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1. Frost, L. H., and Jackson, R. L.: J. Pediat. 39: 585-592, 1951.

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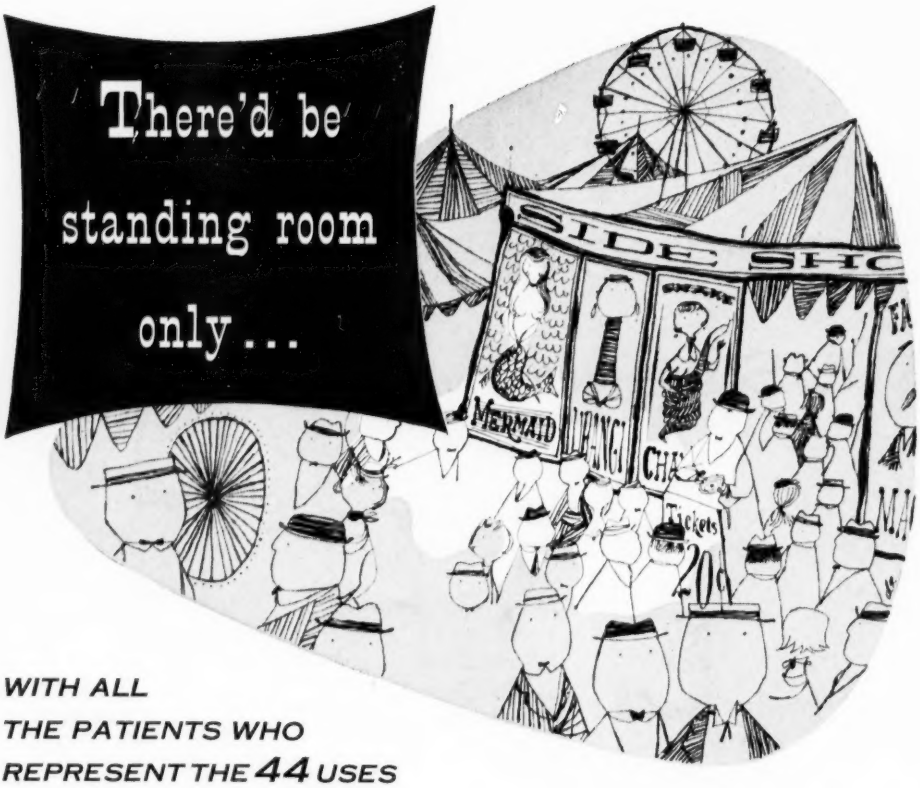

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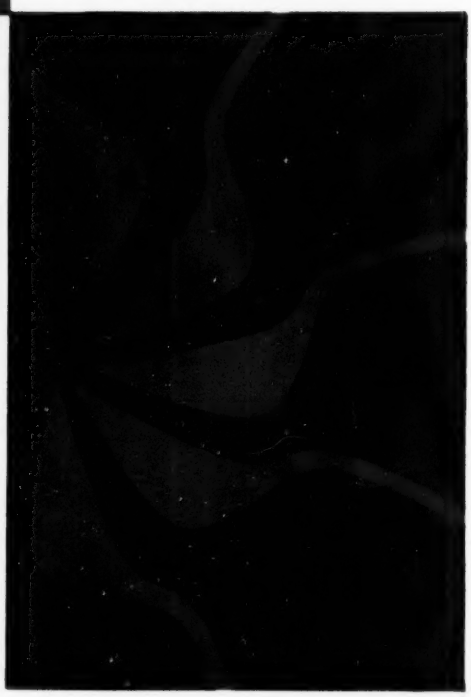

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EFFECT OF SHORT-TERM ADMINISTRATION OF CORTICOTROPIN IN ACTIVE RHEUMATIC CARDITIS

MAY G. WILSON, M.D.
HELEN N. HELPER, M.D.
ROSE LUBSCHEZ, Ph.D.
KATHARINE HAIN, M.D.
AND
NATHAN EPSTEIN, M.D.
NEW YORK

ACTIVE rheumatic carditis is a self-limited process in which the severity of any attack cannot be predicted. The cardiac damage usually sustained in any one attack depends on the duration and the severity of the inflammatory process. This has been demonstrated in both pathological and long-term clinical studies reported by Wilson and other investigators.[1]

It has been shown that certain inflammatory conditions are arrested by the administration of corticotropin (ACTH). Complete termination of self-limited ophthalmological disorders has been reported by Gordon and McLean[2] and by Olson and co-workers.[3] In severe burns, early corticotropin therapy has resulted in decreased inflammation and minimal permanent tissue damage, as reported by Whitelaw.[4]

From these and other observations it was considered that if the acute inflammatory phase of active rheumatic carditis could be terminated by the use of corticotropin before irreversible tissue damage occurred, permanent cardiac damage might be prevented or minimized. This would obviously require the administration of corticotropin as early as possible after the onset of demonstrable active carditis. Because the duration of active carditis is variable, an evaluation of the effect of corticotropin would be simplified by restricting the treatment to a period of time significantly less than its usual course.

From the New York Hospital, Cornell Medical Center, Department of Pediatrics.

This study was aided by grants from the Commonwealth Fund and the Helen Hay Whitney Foundation.

1. Wilson, M. G.: Rheumatic Fever, London, Published for Commonwealth Fund, by Oxford University Press, 1940, p. 145.

2. Gordon, D. M., and McLean, J. M.: Effects of Pituitary Adrenocorticotropic Hormone (ACTH) Therapy in Ophthalmologic Conditions, J. A. M. A. **142**:1271 (April 22) 1950.

3. Olson, J. A.; Steffensen, E. H.; Margulis, R. R.; Smith, R. W., and Whitney, E. L.: Effect of ACTH on Certain Inflammatory Diseases of the Eye, J. A. M. A. **142**:1276 (April 22) 1950.

4. Whitelaw, M. J.: The Treatment of Severe Burns with ACTH: Preliminary Case Reports, in Proceedings of the Second Clinical ACTH Conference, edited by J. R. Mote, Philadelphia, The Blakiston Company, 1951, Vol. 2, p. 310.

In this report, the results of the administration of corticotropin for 4 to 12 days to 28 patients with 32 attacks of active carditis during the years 1949 to 1952 are presented.[5] Control observations made on seven patients who did not receive corticotropin are included for comparison.

MATERIAL AND METHODS

Twenty-eight patients having a total of 32 attacks of active carditis were observed on the pediatric and medical pavilions of The New York Hospital.[6] They ranged in age from 3½ to 18 years. The majority were under observation for a control period of one to nine days, with an average of two days. Patients admitted for treatment with equivocal symptoms or with polyarthritis without demonstrable active carditis were excluded from this study.

A complete physical examination was made daily including weight, blood pressure, vital capacity, and electrocardiogram. An initial blood culture was taken. A complete blood cell count and the sedimentation rate were determined at regular intervals. Twenty-four-hour urine specimens were collected for steroid studies that were done using the methods of Callow and co-workers[7] and Daughaday and co-workers[8]; the results obtained in these and special hematological studies will be reported in a separate communication.

Fluoroscopic examinations in the posteroanterior and oblique views were made daily during the entire period of observation to determine progression and reversal of chamber enlargement. The radioscopic criteria followed have been previously described.[9] The cardiac silhouette in the left oblique view was determined at standard degrees of rotation. In the right oblique view the left auricle was delineated by swallowing barium.

The circulating eosinophile count was determined daily in the fasting state using the method described by Hain,[10] slightly modified.[11] During treatment the circulating eosinophile count was determined each morning at 8 a. m., four hours after an intramuscular injection of corticotropin.

All patients receiving corticotropin were given antibiotic therapy to control intercurrent infections during the study period. The diet was salt-poor and restricted. Fluids were limited to 900 to 1500 cc. Ascorbic acid was administered in doses of 150 mg. daily (Table 1).

Corticotropin[12] was administered intramuscularly every six hours for an average period of seven days. The daily dosage varied from 1 to 5 mg. per kilogram of body weight. For comparative purposes, some patients received corticotropin every eight hours for four to seven days, or the daily dose was gradually decreased during the week of therapy. Three of these patients received a second course of treatment for four to seven days.

---

5. The effect of corticotropin in 11 of these patients was presented in a preliminary report appearing in Proceedings of the Second Clinical ACTH Conference, edited by J. R. Mote, Philadelphia, The Blakiston Company, 1951, Vol. 2, p. 627, and in the J. A. M. A. **145**:133, (Jan. 20) 1951.

6. Five patients were observed on the medical pavilion through the courtesy of Dr. David P. Barr.

7. Callow, N. H.; Callow, R. K., and Emmens, C. W.: Colorimetric Determination of Substances Containing the Grouping-CH_2CO-in Urine Extracts as an Indication of Androgen Content, Biochem. J. **32**:1312 (Aug.) 1938.

8. Daughaday, W. H.; Jaffe, H., and Williams, R. H.: Chemical Assay for "Cortin": Determination of Formaldehyde Liberated on Oxidation with Periodic Acid, J. Clin. Endocrinol. **8**:166 (Feb.) 1948.

9. Wilson,[1] p. 401.

10. Hain, K.: Circulating Eosinophils in Children in Health and Disease. Pediatrics **7**:408 (March) 1951.

11. The Thorn diluting fluid was slightly modified by the addition of 4% propylene glycol. For accuracy it is important to keep both diluting fluid and pipettes chilled during the entire procedure and to shake the filled pipette gently for 30 seconds before filling the counting chamber.

12. Supplied through the courtesy of The Armour Laboratories, Chicago. Since 1951, a special batch allocated for rheumatic fever research has been used.

If the circulating eosinophile count remained between 0 and 10 per cubic millimeter during the period of therapy, the corticotropin dosage was arbitrarily considered to be adequate. When the circulating eosinophile count rose above 10 cells per cubic millimeter, therapy was considered inadequate.

Ten patients presumably had initial atacks of rheumatic fever; 18 had recurrent attacks (a total of 32 episodes). In the majority of patients the duration of active carditis was known. However, for the few patients who had not been followed by us prior to admission the duration of active carditis was estimated from the history. Several patients with active carditis known to be of long duration were included for comparison. With few exceptions, evidence of progressive symptoms and signs of active carditis were observed before therapy was instituted. Seven patients with active carditis of mild degree served as controls.

The following diagnostic criteria were used to determine the presence of progressive symptoms and signs of active carditis: (*a*) the development of new systolic or diastolic murmurs, friction rub, or gallop rhythm; (*b*) progressive enlargement of cardiac chambers on fluoroscopic

TABLE 1.—*Corticotropin Therapy for Seven Days in Active Rheumatic Carditis* *

Criteria to be Followed for Diagnosis	Recommended Dosage Schedule
Development of new murmurs, friction rub, or gallop rhythm, under observation	After Control Period of 1-3 Days
Fluoroscopic evidence of progressive enlargement of cardiac chambers	Corticotropin, I. M., every 6 hr. for 7 days
Evidence of diminishing cardiac reserve, dyspnea, diminishing vital capacity	100 mg./25 mg. for 4 days
ECG evidence of progressive myocardial involvement	80 mg./20 mg. for 3 days
	Other Medication
	Ascorbic acid, 150 mg. daily
Preliminary Examinations	Antibiotic therapy, daily
Blood culture	Diet, 7 Days
R. B. C.—W. B. C.	Salt-poor and restricted
Circulating eosinophiles, 8 a. m.	Fluids limited to 1,000 cc.
Urine	Daily Specific Examinations
Others—when indicated	Circulating eosinophiles†
	Vital capacity
	Fluoroscopy
	ECG
	Blood pressure during therapy

* Associated manifestations of rheumatic fever may or may not be present. Schedule applicable for active carditis of short duration.
† Circulating eosinophiles kept at near zero levels during therapy.

examination in the posteroanterior and oblique views at standard degrees of rotation; (*c*) diminishing cardiac reserve, i. e., dyspnea, decreased vital capacity, and enlarged or tender liver; (*d*) electrocardiographic evidence of myocardial disturbance, i. e., prolongation of P-R interval, A-V dissociation, and T and ST changes.

Active carditis was considered arrested when the signs or symptoms observed during the control period showed no further progression. Active carditis was considered terminated when (*a*) there was fluoroscopic evidence of reversal of chamber enlargement and (*b*) when new murmurs and friction rub disappeared together with reestablishment of a normal cardiac reserve and return of the electrocardiogram to normal. Active carditis was considered to have recurred when any of the manifestations mentioned above were again observed.

Regression and recurrence of associated manifestations of rheumatic fever such as fever, joint pains, arthritis, chorea, and nodules were also noted.

OBSERVATIONS

In Table 2 the observations are summarized for 24 patients receiving adequate corticotropin therapy who had active carditis of less (1 to 9) or more (10 to 19) than 10 days' duration. The severity of active carditis ranged from 1 to 4+. Active carditis was severe or marked in 10 patients and of moderate degree in 14 patients. Observations are also presented for eight patients who received inadequate therapy

TABLE 2.—*Effect of Corticotropin Therapy for Four to Twelve Days in Active Carditis*

Corticotropin Therapy	Total Patient-Courses	Before Therapy: No. Patients	Before Therapy: Progressive Symptoms of Active Carditis: Severity†	Before Therapy: Progressive Symptoms of Active Carditis: Duration, Days	Before Therapy: Other Rheumatic Manifestations,* Duration, Days	After Institution of Therapy: Reversal of Cardiac Enlargement and Return of Normal Cardiac Reserve: No. Patients	After Institution of Therapy: Reversal of Cardiac Enlargement and Return of Normal Cardiac Reserve: Interval, Days	After Discontinuation of Therapy: Recurrences: Carditis: No. Patients	After Discontinuation of Therapy: Recurrences: Carditis: Duration, Days	After Discontinuation of Therapy: Recurrences: Other Rheumatic Manifestations* : No. Patients	After Discontinuation of Therapy: Recurrences: Other Rheumatic Manifestations* : Duration, Days	After Discontinuation of Therapy: Ambulatory Status Attained: No. Patients	After Discontinuation of Therapy: Ambulatory Status Attained: Interval, Wk.	After Discontinuation of Therapy: Cardiac Status Maintained, Interval, Mo.
Adequate‡	24			< 10										
		14	1-4+	1-9	3-28	14	3-9	1	3	2	5-8	14	1-3	3-26
		1	4+	2	3	1	15					1	3	12
				> 10										
		8	1-3+	10-19	9-21	7	2-12	1	7	2	3-8	8	1-3	7-24
		1§	1+									1	3	3
Inadequate‖	8			< 10										
		6	1-4+	3-6	3-7	6	3-5	4 { 3¶ / 1	3-5 / 11			6	1-2	13-29
				> 10										
		2	1-3+	10-14	10-21	1	5	1	14	1	4	2	2-2½	6-18
Total	32	32	1-4+	1-19	3-28	29	2-15	7	3-14	5	3-8	32	1-3	2-29

* Fever, arthralgia, chorea.

† 1+ mild, 2+ moderate, 3+ marked, 4+ severe.

‡ Circulating eosinophiles 0-10/cu. mm. during therapy.

§ Subacute active carditis of several months' duration; no reversal of cardiac enlargement.

‖ Circulating eosinophiles rose above 10/cu. mm. during therapy.

¶ Received second courses of 7 days of corticotropin therapy followed by termination of active carditis and reversal of chamber enlargement with no recurrence.

who had active carditis of less (3 to 6) or more (10 to 14) than 10 days' duration. Active carditis was marked or severe in six patients and of moderate degree in two patients.

Of the 15 patients with active carditis of short duration, 11 had carditis for five days or less. Progressive symptoms and signs of carditis were arrested by the end of the second day of therapy in 14 patients. In one patient who had associated pneumonitis with cyanosis and tachypnea, termination of active carditis was not certain until the ninth day. Fluoroscopic examination on the 15th day revealed reversal of cardiac enlargement. There was termination of active carditis as evidenced by reversal of chamber enlargement in 13 patients. In the majority this occurred by the fifth day, together with the disappearance of new murmurs and friction rub and the restoration of a normal cardiac reserve. One patient had a probable recurrence of minimal carditis associated with fever and anthralgia on the seventh day after therapy was discontinued, which regressed spontaneously in three days. In two other patients, two to eight days after therapy was discontinued, fever and arthritis recurred without overt evidence of active carditis; one of these patients received additional treatment for four days with subsidence of fever and arthralgia. However, subcutaneous nodules which were first noted three days after the end of the first course of treatment persisted for three weeks. It is significant that among 15 patients, five had no resultant enlargement of the cardiac chambers and two had only equivocal enlargement. In six patients whose cardiac status was known before the present illness there was a return to the status noted prior to the attack. In two patients whose previous cardiac status was not known, there was progressive cardiac enlargement before therapy was instituted and there was reversal during therapy. Patients were ambulatory one to three weeks after therapy was completed. During a follow-up period of 3 to 26 months all patients have maintained the cardiac status noted at the end of therapy.

The following three cases demonstrate the clinical course of patients receiving adequate short-term corticotropin therapy.

REPORT OF CASES

W. H. (Fig. 1), 8 years old, received a total of 233 mg. of corticotropin administered intramuscularly during a seven-day period. This was a first attack of moderate severity, characterized by progressive active carditis of two days' duration and associated with arthritis and fever of four days' duration. Symptoms and signs of progressive carditis which included enlarging cardiac chambers, systolic and diastolic murmurs, and diminished cardiac reserve, were arrested by the second day of therapy. Reversal of cardiac chamber enlargement, disappearance of new murmurs, and restoration of normal cardiac reserve occurred by the fifth day of therapy. Fever and arthritis subsided in 24 hours. There was no recurrence, and the patient was ambulatory one week after completion of therapy. Normal cardiac status has been maintained for 15 months.

R. F. (Fig. 2), 8 ½ years old, received a total of 370 mg. of corticotropin administered intramuscularly during a seven-day period. This was a first attack of marked severity, characterized by progressive active carditis of 5 days' duration and associated with fever, joint pains, and arthritis of 14 days' duration. Symptoms of progressive active carditis were arrested by the second day of therapy. Reversal of cardiac chamber enlargement and restoration of normal cardiac reserve were noted on the fifth day of therapy. Fluoroscopic examination on the 11th day revealed a normal cardiac silhouette. Fever and arthritis subsided in 24 hours. There was no recurrence. The patient was ambulatory one week after completion of therapy, and the normal cardiac status observed at the end of therapy has been maintained for two years.

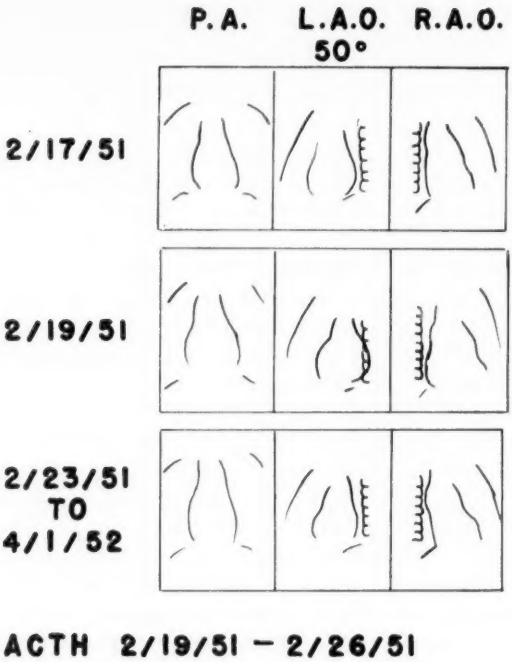

Fig. 1.—Cardiac silhouette for patient W. H. as demonstrated by fluoroscopy before, at the onset, and following corticotropin therapy.

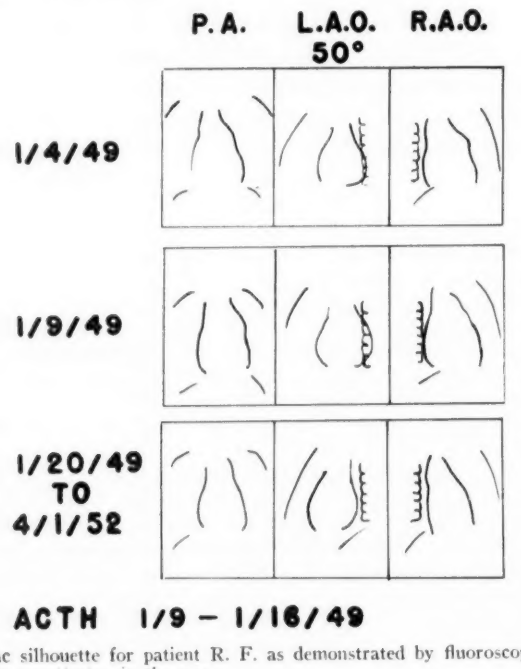

Fig. 2.—Cardiac silhouette for patient R. F. as demonstrated by fluoroscopy before, at the onset, and following corticotropin therapy.

B. F. (Fig. 3), 10½ years old, received a total of 640 mg. of corticotropin administered intramuscularly during a seven-day period. The patient was under medical supervision for two years before the onset of this first attack of rheumatic fever. Arthralgia and fever occurred 12 days prior to therapy. A changing precordial systolic murmur and enlargement of the cardiac chambers were noted nine days before treatment. The symptoms of progressive active carditis were arrested by the second day of therapy, and reversal of cardiac chamber enlargement and return of normal cardiac reserve were attained by the seventh day of therapy. Fever and arthralgia regressed in 24 hours. There was no recurrence, and the patient was ambulatory one week after completion of therapy. The patient has maintained the normal cardiac status noted at the end of treatment for 13 months.

Nine patients with active carditis of 10 to 19 days' duration were considered to have had adequate therapy. Symptoms and signs of progressive carditis were

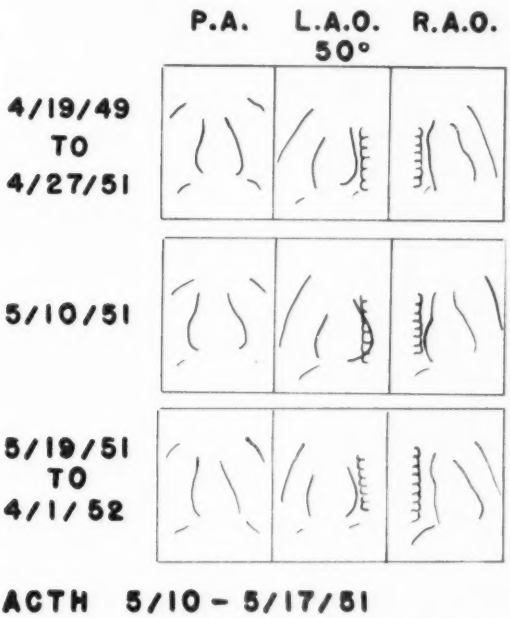

Fig. 3.—Cardiac silhouette for patient B. F. as demonstrated by fluoroscopy before, at the onset, and following corticotropin therapy.

arrested by the third day. There was termination of active carditis with reversal of chamber enlargement and restoration of normal cardiac reserve by the 8th to the 12th day after the start of therapy in seven patients. Two patients with rheumatic carditis of several weeks' duration did not have evidence of progressive enlargement during the control period. In one patient with active rheumatic fever of 19 days' duration, recurrence of active carditis was first noted 10 days after therapy was discontinued. It regressed spontaneously after seven days. Recurrence of associated manifestations of rheumatic fever of three to eight days' duration, without evidence of carditis, occurred in two patients. All patients were ambulatory from one to three weeks after completion of therapy. During a follow-up period of 7 to 24 months these patients have maintained the cardiac status noted at the termination of therapy.

Six patients with active carditis of three to six days' duration were considered to have had inadequate therapy; in four of these, corticotropin therapy was either discontinued or the dosage was reduced for experimental purposes. Progressive symptoms and signs of active carditis were arrested by the third to fourth day of treatment. Termination of active carditis with reversal of chamber enlargement and a return of normal cardiac reserve were noted by the third to fifth day of therapy. One patient, with an initial attack, had no residual cardiac enlargement. There was a recurrence of active carditis of two to seven days' duration in four patients. This was associated with arthritis in one patient. Three of the patients received a second course of therapy. Symptoms of active carditis were terminated

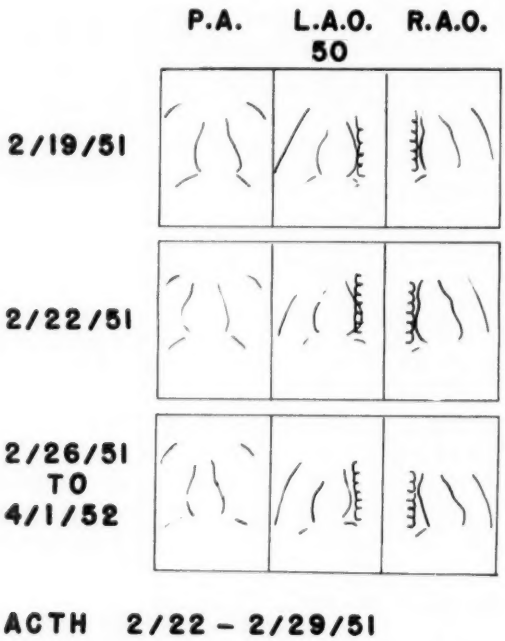

Fig. 4.—Cardiac silhouette for patient K. K. as demonstrated by fluoroscopy before, at the onset, and following corticotropin therapy.

in several days after institution of therapy with reversal of cardiac enlargement and restoration of normal cardiac reserve by the third day. One patient, who did not receive a second course of corticotropin, had a persistent prolongation of the P-R interval for several weeks. During this period he continued to have a normal cardiac reserve and no overt clinical evidence of progressive cardiac damage. During a follow-up period of 13 to 19 months the cardiac status has been maintained as noted at the termination of therapy in these six patients. They were ambulatory in one to two weeks following treatment. The following case demonstrates the clinical course of a patient receiving inadequate therapy.

K. K. (Fig. 4), 6½ years old, received a total of 270 mg. of corticotropin administered intramuscularly during a seven-day period. This was a first attack of mild degree, characterized

by progressive active carditis during 24 hours of observation which was associated with minimal arthritis of three days' duration. By the fourth day of therapy there was reversal of cardiac enlargement to within normal limits and the cardiac reserve returned to normal. Arthralgia subsided in 24 hours. There was no recurrence, and the patient was ambulatory one week after treatment was discontinued. The normal cardiac status noted at the end of therapy has been maintained for 16 months.

Two patients with subacute active carditis of 10 to 14 days' duration were inadequately treated. In one of these, progressive symptoms and signs of carditis were arrested during therapy with reversal of chamber enlargement by the third to fifth day. There was a recurrence of active carditis associated with fever and arthralgia and the appearance of subcutaneous nodules which subsided spontaneously in two weeks. There was equivocal evidence of residual chamber enlargement. In the second patient, no evidence of progressive signs and symptoms of active carditis was observed before therapy and there was no reversal of chamber enlargement after four days of therapy. These two patients were ambulatory two to two and one-half weeks following discontinuation of therapy and have maintained the cardiac status noted at the end of therapy for 6 to 18 months.

Two additional patients are not included in this summary since it is not certain in retrospect whether their cardiac symptoms were due to rheumatic fever.

One patient, a 4½-year-old boy, had an anemia (hemoglobin, 8.9 gm. per 100 cc.) of unknown duration. His present illness was of about 14 days' duration and was characterized by tonsillitis, fever, malaise, and anorexia, for which he received penicillin and sulfonamide therapy. During a five-day control period there was tachycardia, the heart sounds became progressively poorer in quality, and there was an increase in cardiac chamber enlargement. In addition, there was enlargement of the liver and spleen. On adequate corticotropin treatment there was some decrease in cardiac chamber enlargement. Following treatment there was no change in cardiac status and no recurrrence of any symptoms. The liver and spleen did not decrease in size for many months. He responded well to iron therapy. The follow-up period has been one year.

The second child, a 4-year-old boy, presented high fever, chills, petechiae, and questionable neck rigidity of six days' duration. A record of his cardiac status prior to this illness was not available. Because of marked cardiac enlargement and precordial systolic murmur which increased in intensity, he was given adequate corticotropin therapy for one week. Fever, arthralgia, and rash subsided before treatment. There was no significant change in the cardiac status during therapy. He also had a pneumonitis of uncertain nature which was present during the entire period of observation and for several subsequent months. Three months following discharge from the hospital there was an increase in cardiac enlargement.

To illustrate the difficulties inherent in differential diagnosis for patients with polyarthritis without overt clinical evidence of active carditis, observations are included for one patient who was given corticotropin therapy for seven days.

C. K., an 8½-year-old girl, was admitted to The New York Hospital with a history of arthritis and erythema multiforme of several weeks' duration. Examination revealed a basal systolic murmur and equivocal cardiac enlargement. During the control period of observation progressive polyarthritis developed with no change in cardiac status. Within 24 hours after institution of therapy the arthritis and erythema multiforme regressed but recurred three days after therapy was discontinued. During the three-year follow-up period she has exhibited three similar attacks. There was no change in her cardiac status. There were no residual joint changes. Further investigations have suggested that there may be an allergic component in her symptomatology. However, atypical rheumatoid arthritis has not been excluded.

In seven patients with carditis of mild degree who were not treated with corticotropin, the symptoms and signs of active carditis persisted from 10 days to 4 months. There was no reversal of cardiac enlargement in any patient. There was progressive

cardiac enlargement in three patients. In one patient there was equivocal progression. The follow-up period has been from 12 to 15 months. Cardiac silhouettes of four of these patients are presented in Figure 5. Their clinical courses are as follows.

P. W., 10 years of age, was admitted with an initial attack of rheumatic fever of 10 days' duration. During a four-day control period there was no further evidence of progressive active carditis. Adequate salicylate medication was started on the fourth day and given for seven days. The enlargement of cardiac chambers noted on admission persisted for the two-week period of hospitalization and during a 14-month follow-up period.

O'B., 9½ years old, was admitted to the hospital with mild chorea of one day's duration. The cardiac status before this episode was not known. The cardiac chamber enlargement noted on

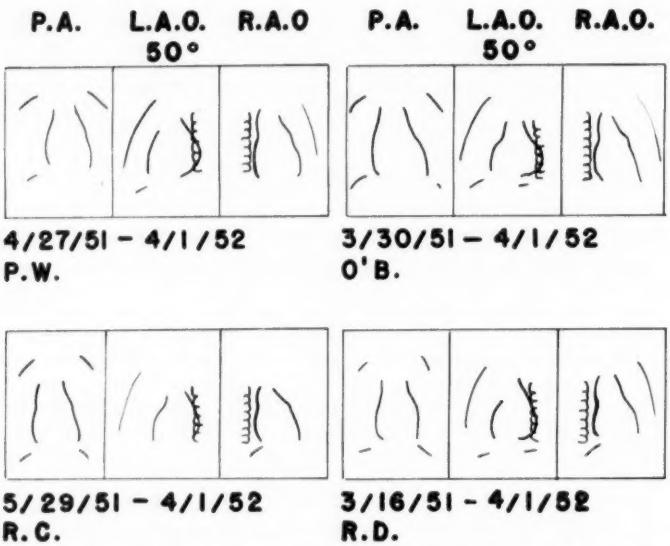

Fig. 5.—Fluoroscopic silhouettes and protocols illustrating the course in four patients who were not given corticotropin and who served as controls.

admission persisted during the seven-day observation period and has remained unchanged during a 15-month follow-up period.

R. C., 8 years of age, was admitted presumably with an initial episode of rheumatic fever of two days' duration. Fever and arthritis subsided spontaneously in 24 hours. The cardiac enlargement noted on admission did not increase but has persisted during a 13-month follow-up period. No therapy was administered.

R. D., 8½ years old, was admitted presumably with an initial attack of rheumatic fever of two days' duration. There was slight progressive enlargement of the cardiac chambers during the early period of hospitalization. Symptoms of rheumatic fever disappeared during the week of observation. The cardiac status has not changed during the 15-month follow-up period.

ADDITIONAL OBSERVATIONS

The electrocardiographic changes noted during therapy are summarized in Table 3 for 34 patient-courses of corticotropin, including two patients who were given a second course of treatment. The mechanism responsible for the bradycardia noted during therapy in 73% of total patient-courses is not clear. It is perhaps of

significance that it was observed in 90% of the patients with severe carditis (Fig. 6). It is also of interest that the bradycardia was observed during the period when the symptoms and signs of progressive carditis were arrested and cardiac chamber enlargement was reversed concomitant with a return of normal cardiac reserve. A normal rate was restored promptly after therapy was discontinued except for two patients in whom it was followed by a relative tachycardia of several days' duration. The increase in amplitude of the T wave in 34% of patient-courses, in the absence of hyperkalemia, is of interest. It has been indicated by Currens and co-workers [13] that the cardiac muscle may have a high potassium content in the presence of a normal serum potassium level.

A comparison of the level of the circulating eosinophiles and the steroid output suggests that the eosinophile count provides a useful index of adrenocortical secretion, as has been generally stated. However, the relative degree of adrenocortical secretion is not necessarily reflected in the circulating eosinophile count. This is illustrated in Figure 7 and in the following case report for patient J. A., who received two seven-day courses of corticotropin therapy. During the first course

TABLE 3.—*Electrocardiographic Changes During a Seven-Day Period of Corticotropin Therapy (437 Tracings in Thirty-Four Patient-Courses)*

Bradycardia	73% of total patient-courses, including 2 patients receiving 2 courses of therapy
Drop of 25 beats/minute or more by 2d to 4th day	90% in patients with severe carditis
P-R interval	35% of total patient-courses
Decrease of 0.04 sec. or more	
T waves	34% of total patient-courses
Increase in amplitude of 3 mm. or more, with peaking (normal serum potassium level)	
P waves	30% of total patient-courses
Decrease in amplitude of 1 mm. or more	

he was given corticotropin which was subsequently discovered to be only 50% of labeled potency.

J. A., a 10½-year-old boy, was under continuous medical supervision since the age of 8 years. He had experienced three previous attacks of rheumatic fever. He was well until Jan. 2, 1951, when he became chilly at school. When taken home he was found to have a temperature of 38.9 C. (102 F.). The next morning he had a slightly stuffy nose and was treated with penicillin until admission. His temperature ranged between 38.9 and 40 C. (104 F.). There were no other symptoms.

On Jan. 5th he first complained of pain in the elbows and ankles and was admitted to the hospital. He had marked pain in the right elbow and ankle. There was no swelling or heat. The pulse rate was 120. There was a systolic murmur which had been heard previously. The heart sounds were of poor quality. On fluoroscopy the base of the heart showed a slight increase in width, and his heart showed very little pulsation. The electrocardiogram revealed slight elevation of the ST segment. During the three-day control period his vital capacity dropped from 2,300 cc. on admission to 1,600 cc. on the second hospital day and to 1,100 cc. on the fourth hospital day, his previous normal being 2,500 cc. On Jan. 6th, the cardiac silhouette on fluoroscopic examination had increased in size in the posteroanterior view with increased chamber enlargement in the oblique views. By Jan. 7th there was progressive electrocardiographic evidence of pericarditis, and by Jan. 10th a friction rub was heard. A diastolic murmur in the 4th and 5th interspaces was audible on Jan. 8th.

13. Currens, J. H., and Crawford, J. D.: The Electrocardiogram and Disturbance of Potassium Metabolism, New England J. Med. **243**:843 (Nov. 30) 1950.

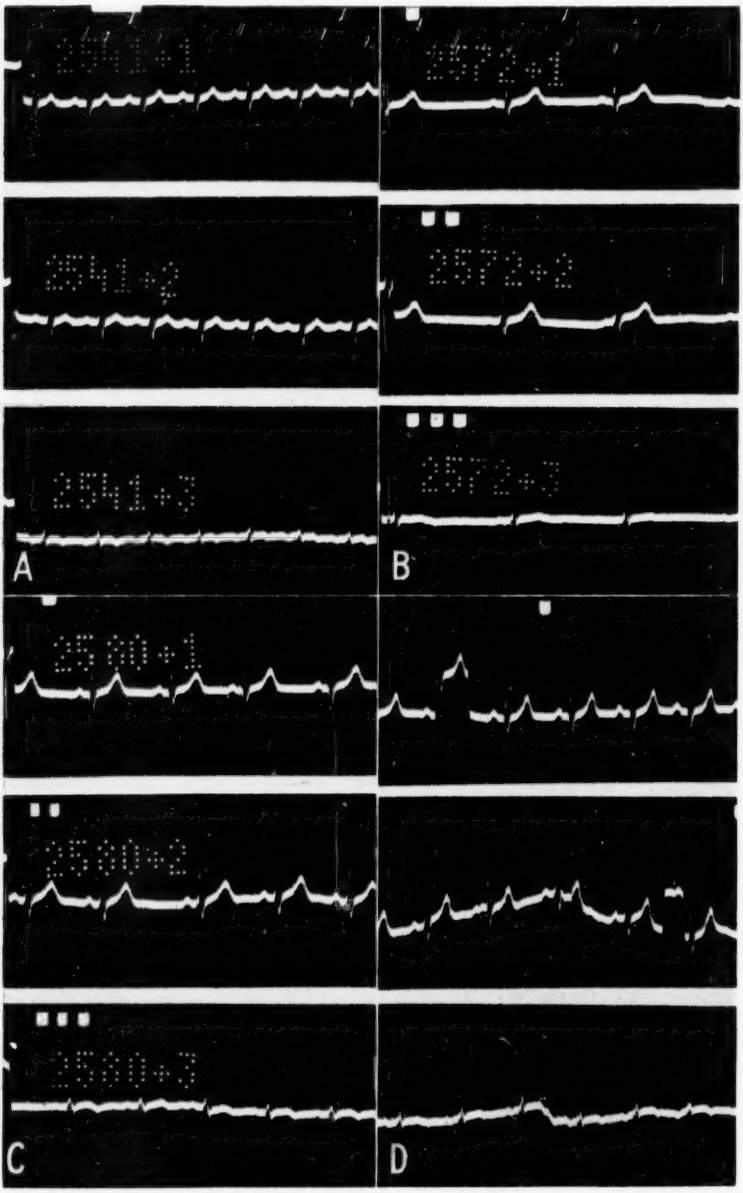

Fig. 6.—Electrocardiographic tracings for patient R. F. *A*, prior to administration of corticotropin. *B*, 48 hours after initiation of corticotropin therapy (sinus bradycardia, increased amplitude of T waves, and decreased amplitude of P waves). *C*, after 96 hours of corticotropin therapy (decreased P-R interval). *D*, 48 hours after treatment was discontinued (rate has increased).

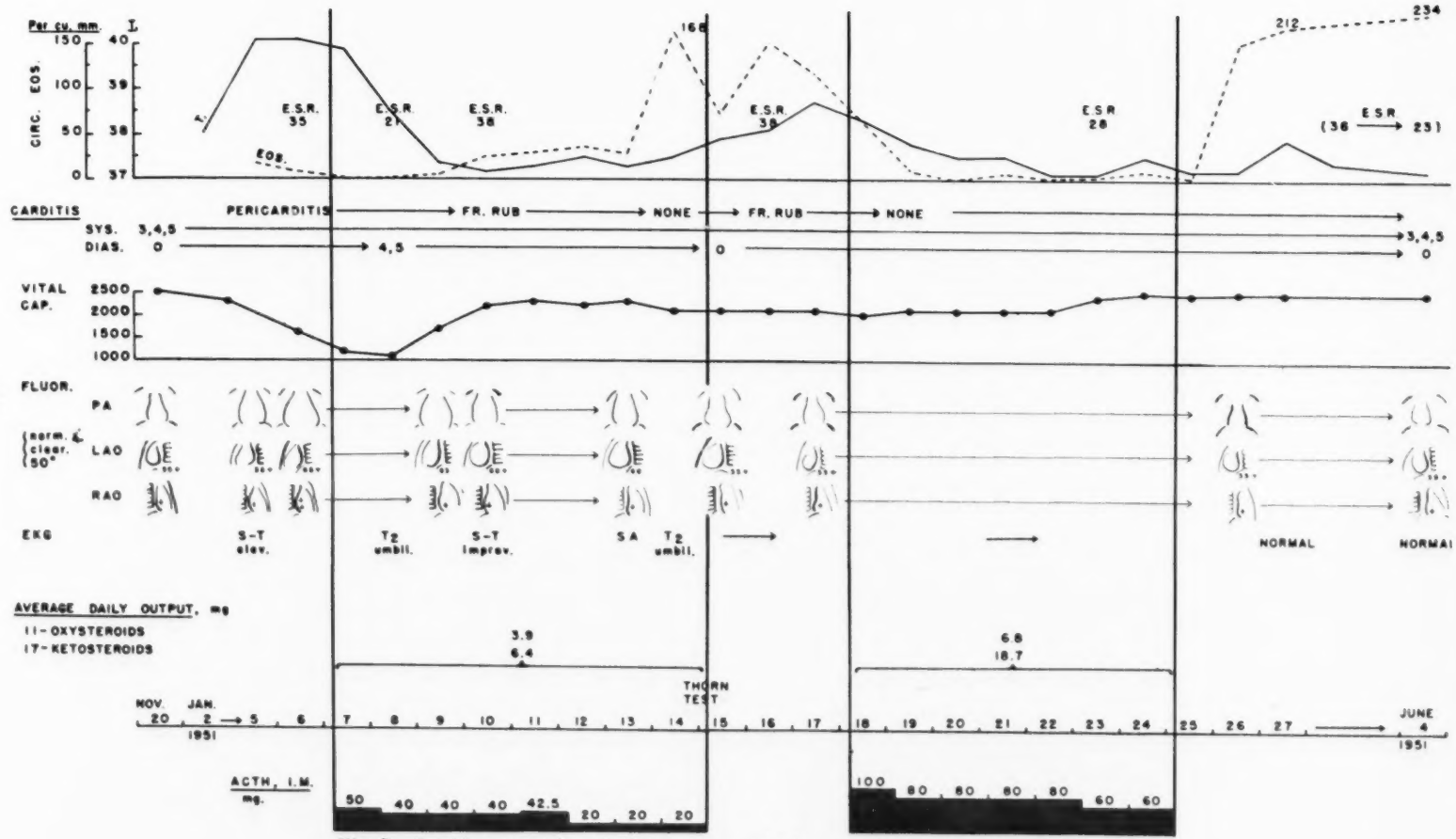

Fig. 7.—Graphic presentation of clinical course and laboratory findings in patient J. A.

Treatment was started on Jan. 7th with corticotropin (special rheumatic-fever-study batch) which later proved to be 50% of the labeled potency. His temperature dropped to normal within 48 hours, and the vital capacity increased to 2,300 cc. by Jan. 13th. Fluoroscopic examination revealed a significant decrease in cardiac size. The friction rub disappeared by the eighth day of therapy.

On Jan. 14th, 24 hours after treatment was stopped, the temperature rose to 38.1 C. (101 F.), the friction rub reappeared, but the cardiac silhouette showed no significant change. Treatment was resumed with another preparation of corticotropin of known potency. The temperature dropped to normal within 24 hours. The vital capacity returned to normal by Jan. 23rd and remained normal. The friction rub disappeared on the second day of therapy. The patient was ambulatory in the fourth week after the onset of illness.

It is important to note that the excretion of 17-ketosteroids and 11-oxysteroids during the second course of therapy was significantly greater than during the first course. A normal Thorn test at this time confirmed our suspicions that the rise in circulating eosinophiles was indicative of inadequate therapy during the first course of treatment. The circulating eosinophiles were 0 to 10 per cubic millimeter before therapy when he had a temperature of 40 C. At this time the 11-oxysteroid and 17-ketosteroid excretions were shown to be 1.4 and 1.5 mg. per 24 hours, respectively. After two days of therapy the eosinophile count was again between 0 and 10 per cubic millimeter, and he excreted 1.6 mg. of 11-oxysteroid and 3.6 mg. of 17-ketosteroid. By the third day of therapy the circulating eosinophile count rose to 26 to 29 per cubic millimeter, and treatment was considered to be inadequate. There was a prompt recurrence of symptoms following discontinuation of therapy. Forty-eight hours after discontinuation of therapy the circulating eosinophile count rose to 103 per cubic millimeter. On reinstitution of therapy with corticotropin of known potency the eosinophile count remained between 0 and 10 per cubic millimeter during the seven-day course. A comparison of the average daily excretion of steroids revealed that the output during the second course was increased three-fold over the first course. These observations indicate that the circulating eosinophile count may be used as a rough index of adrenocortical hormone secretion. However, it is obvious that the relative degree of adrenocortical hormone secretion is not necessarily reflected in the circulating eosinophile count.

This boy experienced a severe attack one year before the recorded episode and another attack after the present one. He received corticotropin during these last three attacks of active carditis, and at present does not reveal any increase in cardiac size over that present before these three episodes.

In summary, it is evident that in all patients with active carditis of short duration the progressive symptoms and signs were arrested during the first few days of corticotropin therapy, regardless of whether the corticotropin dosage was adequate or inadequate. However, in the majority of patients who received inadequate therapy, there was a recurrence of active carditis.

Examination of 24 patients with active carditis who received adequate therapy revealed no overt clinical evidence of increased cardiac damage. There was reversal of chamber enlargement in 22 patients. Two patients with carditis of more than 10 days' duration who did not exhibit progressive cardiac enlargement during the control period showed no reversal of chamber enlargement. All patients were ambulatory within one to three weeks after therapy was discontinued. The cardiac status has been maintained for 3 to 26 months, in the majority for more than 6 months. Two patients had a minimal recurrence of active carditis when therapy was discontinued. There was spontaneous regression in about one week, without evidence of increased cardiac damage. Four patients had a recurrence of other manifestations, i. e., fever and arthralgia, for several days. There was no overt evidence of associated active carditis.

Eight patients had inadequate therapy. Of these, five had a recurrence of active carditis. Three of the latter received a second course of corticotropin in adequate dosage, and in two, carditis regressed spontaneously. Seven patients showed reversal of cardiac enlargement. One patient, with carditis of more than 10 days' duration, did not show progressive enlargement in the control period and did not exhibit reversal of cardiac enlargement. There was no overt evidence of increased residual cardiac damage in these patients, and they were ambulatory from one to two and one-half weeks after therapy was discontinued. They have retained their cardiac status for a period of 6 to 29 months.

COMMENT

Although these observations were made on a limited number of patients with active carditis, they indicate that the short-term administration of corticotropin modifies the natural course of active rheumatic carditis with respect to severity and duration. Overt clinical evidence of increased cardiac damage was not observed. This does not exclude the possibility that minimal cardiac damage was probably sustained. The clinical course observed on corticotropin therapy is in marked contrast to the natural course of active rheumatic carditis. It is not comparable to the course of active rheumatic carditis in patients receiving adequate salicylate therapy. Without hormone therapy, active carditis is of longer duration, and on termination of the rheumatic process there is a demonstrable increase in cardiac chamber enlargement.

In this study, the criteria followed for the estimation of the presence, arrest, or termination of active carditis refer specifically to the cardiac status as determined by physical, fluoroscopic, and electrocardiographic examination. An elevated sedimentation rate alone was not considered evidence of active carditis. The sedimentation rate remained elevated for weeks in the majority of patients when they were ambulatory and had no evidence of diminished cardiac reserve or progressive cardiac damage.

The validity of the use of the circulating eosinophile count as a rough guide to indicate the adequacy of therapy seems to be justified in view of the observations reported. However, on the basis of the urinary excretion of steroids, the relative degree of adrenocortical secretion varied widely when the circulating eosinophile count was 0 to 10 per cubic millimeter.

The mechanism responsible for the termination and reversal of the rheumatic process by corticotropin in an average period of seven days is unknown. The bradycardia noted in the majority of patients and the electrocardiographic findings suggest that the increased production of steroids may have an effect on the myocardium. This possibility is under investigation.

The importance of early treatment is indicated by the failure to obtain reversal of cardiac enlargement in three patients with carditis of longer duration. Of the seven patients in the entire series who experienced recurrent symptoms of active carditis, two did not receive additional therapy. One of these, with active carditis of short duration, showed regression in a few days. The other patient, treated after 14 days, had minimal symptoms for one week. Both patients had no overt evidence of increased cardiac damage. Five patients experienced recurrent symptoms and signs of carditis following inadequate therapy. There was no overt evidence of

increased cardiac damage following a second course of adequate therapy in three of these. Two patients showed spontaneous regression of symptoms of active carditis with persistence of a prolonged P-R interval for several weeks in one.

During the three-year period of study, three patients had recurrent attacks; two patients had two attacks, and one had three attacks. This incidence of recurrence is no greater than would be expected for this age group. It is evident that the use of corticotropin therapy does not reduce the incidence of future recurrences in any patient. It is important to note that patients receiving second and third courses of therapy did not show a difference in response to corticotropin and were not refractory to further therapy.

Since the primary object of this study was to determine whether the progressive symptoms and signs of active carditis could be terminated by corticotropin, treatment was arbitrarily limited to a period of 4 to 12 days, with an average of 7 days. Longer treatment periods would have complicated the evaluation of the efficacy of corticotropin. The observations presented indicate that for patients with carditis of short duration, seven days of adequate therapy will usually be sufficient. Those who experience a recurrence may then receive a second course of adequate therapy. Short periods of treatment decrease the hospital stay and have the obvious advantage that untoward side effects are avoided. Whether administration of smaller doses of corticotropin for a second or third week is of any value cannot be determined by our study. However, in several patients for whom the dosage was gradually decreased during the first week of therapy there was a rise in the circulating eosinophile count, and carditis recurred.

Associated symptoms in all patients, such as fever, arthritis, and erythema multiforme, regressed within 24 to 72 hours following institution of therapy.

SUMMARY AND CONCLUSIONS

Results of the early short-term administration of corticotropin (ACTH) to 28 patients with active carditis in 32 patient courses are presented. These patients have been followed for 3 to 29 months since termination of therapy.

These observations indicate that the administration of corticotropin is followed by arrest and termination of active carditis without overt clinical evidence of residual cardiac damage. This has been attributed to the early use of corticotropin before irreversible damage is sustained. The natural course of active carditis was favorably altered by decreasing both the severity and the duration of the attack.

525 E. 68th St. (Dr. Wilson).

GROWTH AND METABOLISM IN NORMAL AND THYROID-ABLATED INFANT RHESUS MONKEYS (MACACA MULATTA)

III. Growth and Metabolism Following *l*-Thyroxine Administration in Thyroid-Ablated Infant Rhesus Monkeys (Macaca Mulatta)

DONALD E. PICKERING, M.D.
AND
DELBERT A. FISHER, M.D.
SAN FRANCISCO

AS ONE integral in a series of associated studies and reports upon growth and metabolism in normal and athyroid infant macaque monkeys,[1] this communication presents investigations with athyroid infants during short- and long-term periods of therapy with *l*-thyroxine.

Previously reported studies dealing with such therapy in the athyroid macaque monkey are limited to observations upon surgically thyroidectomized adult animals.[2] Fleischmann and co-workers [2a] observed that creatinuria and a drop in serum cholesterol followed administration of 1.0 mg. of thyroxine to such animals, either before or after surgical thyroidectomy, and that when one of their thyroidectomized animals was given a similar dose its basal metabolic rate increased from 44.1 to 56.8 calories per kilogram of body weight per day. Jailer and co-workers [2b] also observed a creatinuria and drop in serum cholesterol in two normal and two sur-

From the Department of Pediatrics and Pediatric Section of the Metabolic Unit of the University of California Medical School.

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1. (*a*) Pickering, D. E.; Smyth, F. S.; van Wagenen, G., and Fisher, D. A.: Growth and Metabolism in Normal and Thyroid-Ablated Infant Rhesus Monkeys (Macaca Mulatta): I. Growth and Metabolism in Normal Infant Rhesus Monkeys (Macaca Mulatta), A. M. A. Am. J. Dis. Child. **86**:1, 1953. (*b*) Pickering, D. E., and Fisher, D. A.: II. Growth and Metabolism in Thyroid-Ablated Infant Rhesus Monkeys (Macaca Mulatta), ibid. **86**:11, 1943. (*c*) Pickering, D. E.; Fisher, D. A., and Scott, K. G.: IV. Radiosodium (Na^{24}) Space in Normal and Thyroid-Ablated Infant Rhesus Monkeys (Macaca Mulatta), ibid., this issue, p. 157. (*d*) Lusted, L.; Pickering, D. E.; Fisher, D. A., and Smyth, F. S.: V. Roentgenographic Features of Skeletal Development in Normal and Thyroid-Ablated Infant Rhesus Monkeys (Macaca Mulatta), ibid., to be published. (*e*) Pickering, D. E.; Fisher, D. A., and Scott, K. G.: VI. Iodine Metabolism in Normal and Thyroid-Ablated Infant Rhesus Monkeys (Macaca Mulatta), ibid., to be published. (*f*) Crane, J.; Pickering, D. E., and van Wagenen, G.: VII. Histopathology of Normal and Thyroid-Ablated Infant Rhesus Monkeys (Macaca Mulatta), to be published.

2. (*a*) Fleischmann, W.; Shumacker, H. B., Jr., and Straus, W. L., Jr.: Influence of Age on the Effect of Thyroidectomy in the Rhesus Monkey, Endocrinology **32**:238, 1943. (*b*) Jailer, J. W.; Sperry, W. M.; Engle, E. T., and Smelser, G. K.: Experimental Hypothyroidism in the Monkey, Endocrinology **35**:27, 1944.

gically thyroidectomized adult animals treated with 0.25 mg. of thyroxine daily for 10 days. The similarity of reactions precipitated by thyroxine in normal and athyroid animals no doubt reflected the magnitude of doses given. In the presently reported studies following the single administration of 0.25 mg. per kilogram of body weight, serum butyl-extractable iodine values of normal and/or athyroid animals reached a level six to seven times greater than normal.

In addition to describing physical, behavioral, and metabolic effects of a single injection of *l*-thyroxine, the present report details variations in metabolic and growth responses associated with long-term (four months) administration.

METHODS AND MATERIALS

All animals were rendered athyroid by I^{131} thyroid ablation at the following ages: Animal A-791 at 22 days, Animal P-790 at 35 days, Animal B-767 at 162 days, and Animal S-775 at 122 days.[1b] Completeness of thyroid ablation was ascertained in each case by studies demonstrating an absence of I^{131} concentration in the anatomical regions of their thyroids, serum butyl-extractable iodine levels which were reduced from normal (4 to 8 γ per 100 cc.) to the low values of 0 to 1 γ per 100 cc., and, finally, lack of gross and/or histological evidence of thyroid tissue in Animals A-791 and S-775 when they were electively killed at a later date.[3] All animals studied were free from physical and biochemical signs commonly associated with hypoparathyroidism,[1b] and viable parathyroid glands were identified histologically in those animals killed.[1f]

Care, feeding, and metabolic study techniques employed have been described,[4] and butyl-extractable iodine determinations were performed by the techniques also described in another communication.[1e] Caloric nitrogen, calcium, and phosphorus intakes were calculated throughout the study; in addition, 72-hour balance studies were conducted at designated intervals. Urinary creatine and creatinine were determined on the same excreta. Frequent weighings and general examinations were made on each animal, and full-body roentgenograms were taken at monthly intervals.[1d]

A sterile solution of *l*-thyroxine sodium in propylene glycol containing 1.0, 0.6, or 0.2 mg. per cubic centimeter was administered intramuscularly (provided through the courtesy of Dr. H. Roebling Knock, Director of Specialty Division, Smith, Kline & French Laboratories, Philadelphia).

Doses of *l*-thyroxine employed in the long-term studies were selected to bring out the differential between the daily amount required to meet general metabolic needs and the anticipated requirements necessary for reestablishment of skeletal growth and maturation and maintenance of normal serum butyl-extractable iodine level. Dosages were computed from data presented in Figure 1, as follows: It was assumed that within 10 days the 0.25 mg. per kilogram of body weight of thyroxine administered had undergone diffusion throughout its potential body compartment and was reflected by the serum butyl-extractable iodine level at that time. Twteny-four hours following injection of 0.25 mg. per kilogram in normal and/or athyroid animals, butyl-extractable iodine levels were $40 \pm \gamma$ per 100 cc. From investigations employing I^{131}-labelled thyroxine, this level was considered to reflect approximately 90% of the given dose. A proportionate value of 15 to 20% of the original dose ($50 \pm \gamma$ per kilogram) was assigned the 10-day serum level of 6 to 8 γ per 100 cc. Since that value had dropped to the pretreatment level within an additional 10 days, thyroxine utilized was assumed to be approximately 5 γ per kilogram per day. In the absence of bone growth following such therapy,[1d] thyroxine so utilized was considered to represent that chiefly capable of serving needs of metabolic activity in tissues other than bone. In two animals studied (Table 1) 20 γ per kilogram per day was considered adequate for maintenance of normal metabolic activity plus requirements incident to the reinstitution of normal skeletal growth and development. The dose of 6 γ per kilogram per day, given one animal, was calculated to supply only that thyroxine required of general metabolic activity.

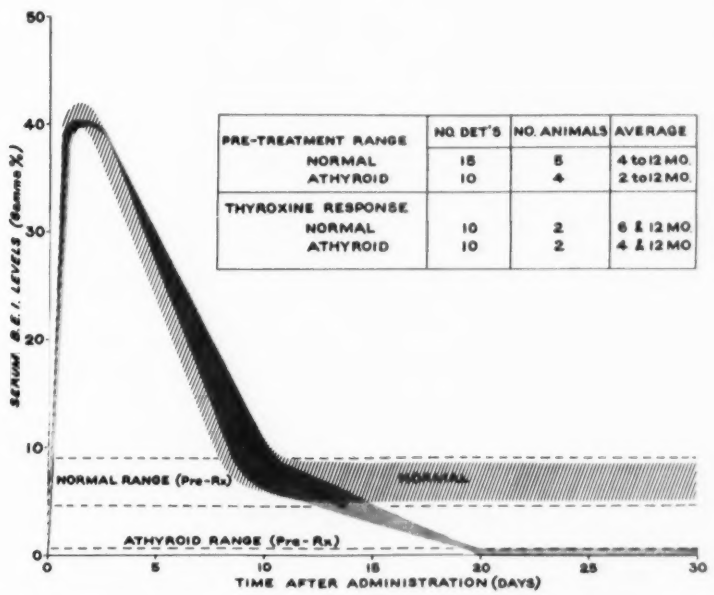
3. Footnotes 1 *b*, *e*, and *f*.

4. Footnotes 1 *a* and *b*.

RESULTS AND COMMENT

Administration of a single dose of 0.25 mg. per kilogram of *l*-thyroxine to normal and/or athyroid macaque monkeys precipitated an immediate and transient increase in the serum butyl-extractable iodine levels to approximately 40 γ per 100 cc. That level dissipated to the normal range (4 to 8 γ per 100 cc.) in 10 days. While levels in the euthyroid animals thereafter remained normal, in the athyroid animals they fell to pretreatment levels of 0 to 1 γ per 100 cc. by 20 days (Fig. 1).

All athyroid animals underwent transient physical, behavioral, dietary, and metabolic changes during the post-treatment period. They also experienced a 10+% loss in body weight within 3 to 6 days, followed by a transient weight gain.



PRE-TREATMENT RANGE	NO. DET'S	NO. ANIMALS	AVERAGE
NORMAL	18	8	4 to 12 MO.
ATHYROID	10	4	2 to 12 MO.
THYROXINE RESPONSE			
NORMAL	10	2	6 & 12 MO.
ATHYROID	10	2	4 & 12 MO.

Fig. 1.—Serum butyl-extractable iodine levels after administration of *l*-thyroxine in normal and athyroid macaque infants.

These changes were associated with increased activity and voluntary food intake as well as a transient reversal of certain physical and metabolic signs of athyrosis. There was significant decrease in postural and behavioral attitude of crouching and withdrawal, as well as a reversal of physical features secondary to myxedema. No appreciable change from the pretreatment skeletal picture occurred.[1d]

Transient metabolic changes were chiefly limited to increased retention of nitrogen and a short-lived creatinuria. Data from balance studies in two of the animals treated are reported in Table 1.

Following therapy, nitrogen retention in Animal A-791 underwent a 100% increase by 15 to 18 days, with a similar effect in Animal S-775. Calcium and phosphorus retentions in either animal underwent only minor changes following therapy.

In Table 2 data are presented relative to changes in the urinary excretion of creatine and creatinine following therapy.

Studies conducted in these athyroid animals during the pretreatment period had already shown that urinary excretion of creatine and creatinine was significantly reduced from normal.[1b] When studied one to four days after therapy,

TABLE 1.—*Nitrogen-, Calcium-, and Phosphorus-Balance Following the Single Injection of l-Thyroxine in Athyroid Macaque Infants**

	Study Period, Days		72-Hr. Balance Data, Mg./Kg./Day								
			Nitrogen			Calcium			Phosphorus		
Animal	Before Rx	After Rx	Intake	Output	Balance	Intake	Output	Balance	Intake	Output	Balance
A-791	6-3	.....	552	270	282	110	38.8	71	90	35.9	54
	...	15-18	850	282	568	164	86.9	77	138	83	55
	...	36-39	518	223	295	102	79	23	85	59	26
S-775	24-21	.....	490	253	237	92.5	58.3	34	79.9	58.1	22
	.....	15-18	548	113	435	99.7	46.4	53	88.5	39.6	49

* 0.25 mg./kg. body weight.

TABLE 2.—*Urinary Creatine and Creatinine Excretion Following the Single Injection of l-Thyroxine in Athyroid Macaque Infants**

	Study Period, Days		Excretion Data, Mg./Kg./Day		
Animal	Before Rx	After Rx	Creatine	Creatinine	Creatine Creatinine
A-791	6-3	.....	6.1	12.2	1:2.0
	...	15-18	3.0	13.1	1:4.4
	...	36-39	5.7	12.9	1:2.3
S-775	24-21	.....	3.1	6.6	1:2.1
	...	15-18	0.9	8.32	1:9.3
B-767	1-4	.....	30.8	16.3	1.9:1
	...	26-29	2.7	16.7	1:6.2
P-790	...	26-29	2.0	10.2	1:5.0
	...	38-41	3.3	7.7	1:2.3

* 0.25 mg./kg. body weight.

TABLE 3.—*Long-Term l-Thyroxine Therapy Schedule*

	Age During Treatment, Days		
Animal	Onset	End	l-Thyroxine Given, γ/Kg./Day
A-791	153	243	20
B-767	317	428	20
P-790	167	257	6

Animal B-767 underwent a marked increase in urinary creatine excretion to 30.8 mg. per kilogram of body weight per day. This effect was not observed in the studies conducted 15 or more days after injection of thyroxine. This confirms the observations of Fleischmann and co-workers [2a] and Jailer and co-workers [2b] that a profound but short-lived creatinuria was observed to follow short-term administration of large doses of thyroxine.

Data obtained during long-term replacement therapy will next be presented (Table 3), representing dosage schedules employed with various animals studied.

All animals began to undergo measurable progression toward normal physical appearance within 15 to 20 days following the onset of therapy. General activity, curiosity, and socialization were essentially normal within this period, as were postural attitudes and muscle tone. The athyroid infants experienced a characteristic profound drop in body temperature when placed in a cold room [1b]; however, their

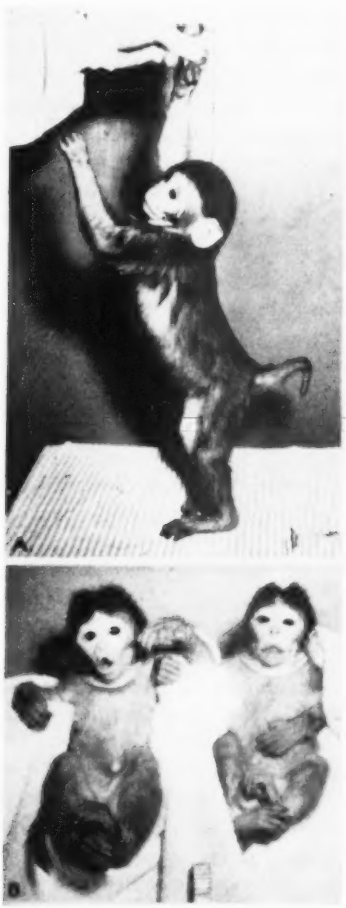


Fig. 2.—*A*, athyroid macaque infant A-791 after two months of "optimal" therapy with *l*-thyroxine. *B*, right, athyroid macaque infant (A-791); left, athyroid macaque infant (P-790) before therapy.

body temperature and its control returned to normal after therapy. Within 30 to 45 days their scaly and somewhat thickened skins, falling in folds over their faces and necks,[1b] became indistinguishable from normal skin. Simultaneously, their coarse dull hair, which had not followed body contour, returned to normal with a regrowth of the hair previously lost over their tails and forearms. Their umbilical hernias also disappeared. Hoarse voices, profound macroglossia, and associated palatoglossal

and palatopharyngeal arch enlargement disappeared within 30 to 45 days. Eruption of deciduous teeth, quiescent during the pretreatment period,[1b] occurred at a rapid rate following therapy.

Features described above are presented in Figure 2. In that figure, "Animal A" was photographed two months after institution of therapy, while "Animal B (right)" is the same animal one month before onset of therapy. Photographs were proportionately scaled.

Data relative to rates of body weight gain and voluntary nutritional intakes for Animals A-791 and P-790 during the period of therapy are presented in Figure 3.

It will be observed that each animal, after initially experiencing the transient weight loss associated with clearing of myxedema, began to gain weight by 5 to 10 days and thereafter continued at an increasingly accelerated rate. Simultaneously, their caloric, nitrogen, calcium, and phosphorus intakes increased at rates paralleling their rates of body weight gain. Similar data for Animal B-767 are presented below, Figure 4.

Following the transient weight loss and associated clearing of myxedema, body weight gain began 10 days after the onset of therapy and continued at an increasingly accelerated rate. Intake of calories, nitrogen, calcium, and phosphorus also increased. The strikingly parallel interrelationships shown between rates of weight gain and voluntary intakes were very similar to these entities in normally growing infants.[1b]

Metabolic balance studies were conducted at varying intervals during therapy and are presented in Table 4.

In each of the animals studied, retentions of nitrogen and phosphorus progressively increased over the period of therapy, while calcium retention was approximately 50 to 60% of that which would be expected in normal infants undergoing similar growth and nitrogen and phosphorus retentions.[1a] Paradoxically, that phenomenon was least marked in Animal P-790, which received the smaller dose of 6 γ per kilogram per day of *l*-thyroxine.

Features of skeletal growth and reorganization in these animals serve, in part, to make tenable the described deficit in calcium retention, which would not normally be expected in light of observed weight gain, and nitrogen and phosphorus retentions in the treated animals. All athyroid animals, during the pretreatment period (four months), underwent insignificant linear bone growth with low but significant calcium retention (25 to 50 mg. per kilogram per day). In conjunction with this, their bones became dense (1.6 times normal).[5] Histological examination of skeletal tissue revealed this to be related to faulty bone reorganization.[2a] It follows, therefore, that considerable calcium was made available to the metabolic pool with the reinstitution of bone reorganization. Serial roentgen surveys conducted during the period of study revealed evidence of active resumption of linear bone growth to a near normal rate together with bone reorganization.[1d] In contrast, in Animal P-790, though increased from the pretreatment levels, bone reorganization as well as linear bone growth were less marked than in Animal A-791. Calcium made available by bone reorganization in these animals must, therefore, have partially served the calcium requirements obviated by resumption of active bone growth and not met by observed calcium retentions.

5. Footnote 1*a* and *d* and 2*a*.

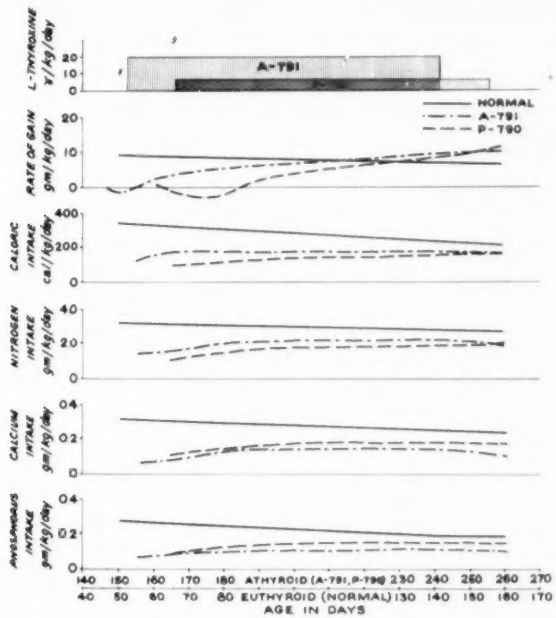


Fig. 3.—Rate of gain and nutritional intake in normal versus thyroxine-treated athyroid macaque (A-791, P-790).

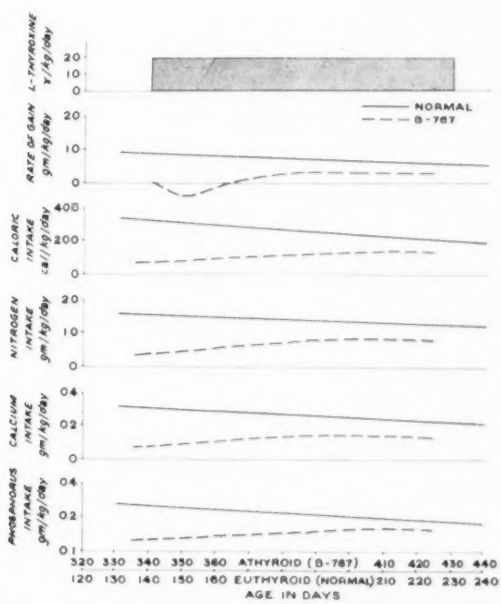

L-THYROXINE γ/kg/day
NORMAL
B-767
RATE OF GAIN gm/kg/day
CALORIC INTAKE cal/kg/day
NITROGEN INTAKE gm/kg/day
CALCIUM INTAKE gm/kg/day
PHOSPHORUS INTAKE gm/kg/day
320 330 340 350 360 ATHYROID (B-767) 410 420 430 440
120 130 140 150 160 EUTHYROID (NORMAL) 210 220 230 240
AGE IN DAYS

Fig. 4.—Rate of gain and nutritional intake in normal versus thyroxine-treated athyroid macaque (B-767).

These relationships among nitrogen, calcium, and phosphorus retention are graphically presented, together with creatine-creatinine excretion data, in Figure 5.

It will be recalled that in normal and athyroid animals a profound short-lived creatinuria follows administration of thyroxine in quantities sufficient to produce serum butyl-extractable iodine levels 6 to 8 times greater than those found in euthyroid animals. Such a creatinuria is no doubt precipitated by transient thyrotoxicosis. Such data, therefore, contribute little knowledge on the effects of

TABLE 4.—*Metabolic Response to Long Term l-Thyroxine Therapy in Infant Macaque Monkeys*

Metabolic Data, Mg./Kg./Day	Before Rx	72-Hr. Balance Studies After Treatment				
Animal A-791	17-14 Days	0-3 Days	4-7 Days	8-11 Days	72-75 Days	79-82 Days
Nitrogen						
Intake	518	643	708	880	1,000	1,100
Output	223	227	379	310	549	503
Balance (+)	295	416	329	570	451	597
Calcium						
Intake	102	122	133	170	192	213
Output	79	58.6	82.9	120.4	189.6	162.6
Balance (+)	23	63	50	50	2	50
Phosphorus						
Intake	85	104	114	143	162	177
Output	59	36.9	74.6	67.5	56.6	42.4
Balance (+)	26	67	39	75	105	135
Urinary						
Creatine	5.72	22.5	22.2	13.6	9.57	10.4
Creatinine	12.9	13.1	13.5	11.4	25.8	20.9
Animal P-790	4-1 Days	0-3 Days	4-7 Days	8-11 Days	72-75 Days	79-82 Days
Nitrogen						
Intake	590	676	773	696	1,130	830
Output	230	169.5	221.8	123.5	406	...
Balance (+)	360	506	551	572	724	...
Calcium						
Intake	112	132	156	160	220	166
Output	65.6	85.9	78.3	62.8	146.2	...
Balance (+)	46	46	78	97	74	...
Phosphorus						
Intake	95.6	100	127	129	183	135
Output	50.8	32.4	59	40.4	50.9	...
Balance (+)	45	68	68	89	132	...
Urinary						
Creatine	6.6	15.2	10.2	5.0	5.1	5.8
Creatinine	11.9	7.7	6.6	4.2	16.2	23.2

physiological quantities of thyroxine in the euthyroid subject. For that reason, urinary creatine-creatinine studies were made during the long-term studies, with doses given Animals A-791, P-790, and B-767. In each case, the doses given precipitated normal physiological responses to over-all growth and metabolism. Such studies revealed that those doses similarly precipitated a transient and profound short-lived creatinuria, followed by plateaued creatine excretion at approximately the normal level of 6 to 10 mg. per kilogram per day. Creatinine excretion remained unchanged during the period of creatinuria (0 to 10 days), and then increased to normal levels (20 ± 5 mg. per kilogram per day) by 75 days.

After cessation of therapy in all animals, growth ceased, and they reverted to their pretreatment physical and metabolic status by 30 to 45 days.

In summary, administration of *l*-thyroxine over a four-month period resulted in the reversal of pretreatment physical and behavioral athyroid characteristics, the resumption of increase in rates of body weight gain to normal rates together with corresponding increase in voluntary food intake and increased retentions of nitrogen and phosphorus. Animals receiving a dose of 20 γ per kilogram per day also resumed normal skeletal growth and development, while the animal receiving 6 γ per kilogram per day lagged considerably in this respect. Calcium retention in both groups was less than expected, presumably because of calcium made available by reorganization of overly calcified bone. An immediate and profound short-lived

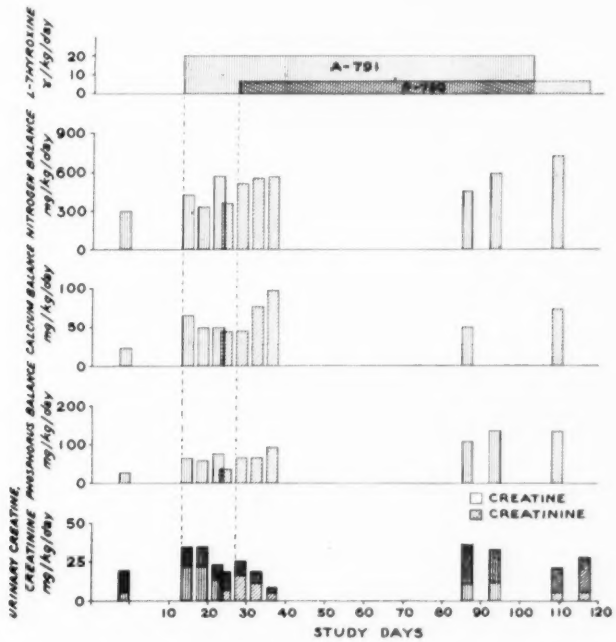


Fig. 5.—Metabolic response to long-term *l*-thyroxine treatment in macaque infants.

creatinuria followed the onset of treatment. Creatinine excretion gradually returned to normal by 75 days.

CONCLUSIONS

Responses of four athyroid infant macaque monkeys to *l*-thyroxine administration were investigated. Two types of studies were conducted: (*a*) the responses to the single injection of 0.25 mg. per kilogram, and (*b*) over-all and differential responses to prolonged therapy with 20 γ per kilogram per day and 6 γ per kilogram per day.

Significant changes followed the single dose and were limited to a transient clearing of myxedema, subsequent transient weight gain and associated increased voluntary food intake, increased positive nitrogen balance, and profound but short-lived creatinuria.

With long-term therapy, all animals underwent a return to normal physical and behavioral features by 30 to 45 days. Myxedema cleared by 10 days, followed by an accelerated rate of body weight gain with increased voluntary food intake and significantly augmented nitrogen and phosphorus retentions.

Following long-term therapy, creatinuria was immediate and profound and limited to the first 10 days, while creatinine excretion slowly returned to normal levels of 20 ± 5 mg. per kilogram per day by 75 days in all animals.

Following therapy, calcium retention did not increase proportionately with that of nitrogen and phosphorus. The difference between the observed and anticipated retention was felt to be related to calcium made available by reorganization of the overly calcified bone characteristic of the pretreatment athyroid animal.

Margaret Cole and Mary Gaylord gave technical assistance in this study.

GROWTH AND METABOLISM IN NORMAL AND THYROID-ABLATED INFANT RHESUS MONKEYS (MACACA MULATTA)

IV. Radiosodium (Na^{24}) Space in Normal and Thyroid-Ablated Infant Rhesus Monkeys (Macaca Mulatta)

DONALD E. PICKERING, M.D.
DELBERT A. FISHER, M.D.
AND
KENNETH G. SCOTT, Ph.D.
SAN FRANCISCO

THE PURPOSE of this communication is to relate Na^{24} "space" data with previously reported growth and metabolic studies in normal and thyroid-ablated infant macaque monkeys.[1]

Na^{24} "space" was sought as a measure of one relatively constant increment of total body mass and was determined at varying intervals during growth and compared in normal and myxedematous subjects.

METHODS

Techniques of animal care and feeding have been reported in a previous communication.[1a] Radiosodium (Na^{24}) was procured from the Oak Ridge National Laboratory, where it was prepared by neutron bombardment of sodium carbonate. The half-life of Na^{24} is 14.9 hours. Samples received in this laboratory were prepared as isotonic sterile solutions and diluted with 0.85% NaCl to contain approximately 10 μc per cubic centimeter at the time of animal injection.

From the Department of Pediatrics (Dr. Pickering and Dr. Fisher) and the Radioactivity Research Center (Dr. Scott), University of California Medical School.

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1. (*a*) Pickering, D. E.; Smyth, F. S.; Van Wagenen, G., and Fisher, D. A.: Growth and Metabolism in Normal and Thyroid-Ablated Infant Rhesus Monkeys (Macaca Mulatta): I. Growth and Metabolism in Normal Infant Rhesus Monkeys (Macaca Mulatta), A. M. A. Am. J. Dis. Child. **86**:1, 1953. (*b*) Pickering, D. E.; Fisher, D. A., and Smyth, F. S.: II. Growth and Metabolism in Thyroid-Ablated Infant Rhesus Monkeys (Macaca Mulatta), ibid. **86**:11, 1953. (*c*) Pickering, D. E., and Fisher, D. A.: III. Growth and Metabolism Following *l*-Thyroxine Administration in Thyroid-Ablated Infant Rhesus Monkeys (Macaca Mulatta), ibid., this issue, p. 147. (*d*) Lusted, L.; Pickering, D. E.; Fisher, D. A., and Smyth, F. S.: V. Roentgenographic Features of Skeletal Development in Normal and Thyroid-Ablated Infant Rhesus Monkeys (Macaca Mulatta), ibid., to be published. (*e*) Pickering, D. E.; Fisher, D. A., and Scott, K. G.: VI. Iodine Metabolism in Normal and Thyroid-Ablated Infant Rhesus Monkeys (Macaca Mulatta), ibid., to be published. (*f*) Crane, J.; Pickering, D. E., and Smyth, F. S.: VII. Histopathology of Normal and Thyroid-Ablated Infant Rhesus Monkeys (Macaca Mulatta), ibid., to be published.

The quantity of isotope present in samples was determined with a scintillation counter. This was composed of a No. 5819 photomultiplier tube and a thallium-activated sodium iodide crystal 2 cm. in thickness. Emitted beta particles were filtered by an aluminum disk interposed between the crystal surface and samples. Na^{24}-containing samples were placed 1 cm. from the crystal surface for counting. Approximately 10% of gamma particles resulting from Na^{24} decay were observed as counts. Correction for mass absorption in the samples measured was obviated by counting gamma rays only.

The counting tube was shielded with sufficient lead to keep the background below two counts per second, and in all samples sufficient counts were observed to keep statistical fluctuation below 3%. All biological fluid samples and standards were appropriately diluted to contain approximately 40 counts per second per gram before being counted. Aliquots were further diluted to 5 cc. with 0.85% NaCl and counted in an open-faced flat cup measuring 4.5 cm. in diameter and 1 cm. in depth.

Each animal received 0.5 cc. per kilogram of body weight of the Na^{24}-containing solution intraperitoneally. From the same syringe 1 cc. samples were delivered into volumetric flasks and diluted to 500 cc. with 0.85% NaCl. These served as the radiosodium standards from which total injected counts were determined. Urinary excretion of Na^{24} was determined during the period of study. Plasma samples were drawn and prepared for counting at intervals of 2, 5,

Fifteen- to Sixteen-Hour Na^{24} Space

Animal	Sex	Age, Days	Weight, Gm.	Na^{24} Space, as % Body Weight
D-766	Male	48	947	38.2
		152	1,830	37.6
B-767	Female	46	954	39.6
		151	1,800	36.0
S-775	Female	18	545	47.0
		121	1,380	36.0

15 to 16, and 24 hours following intraperitoneal administration of Na^{24}. These weighed samples were counted with the radiosodium standards and urine aliquots at the termination of each study. By counting the standard and biological samples at the same time any correction for decay or sensitivity of the measuring instrument was cancelled out. The total Na^{24} counts given, less the total counts excreted in urine, represented Na^{24} available (as total counts) for diffusion in body fluid. According to the formula of Bowers and Scott,[2] the count per second per gram of plasma was then divided into the total counts available for diffusion, and thus the Na^{24} space in grams was determined. This was further converted to per cent of body weight for presentation of data.

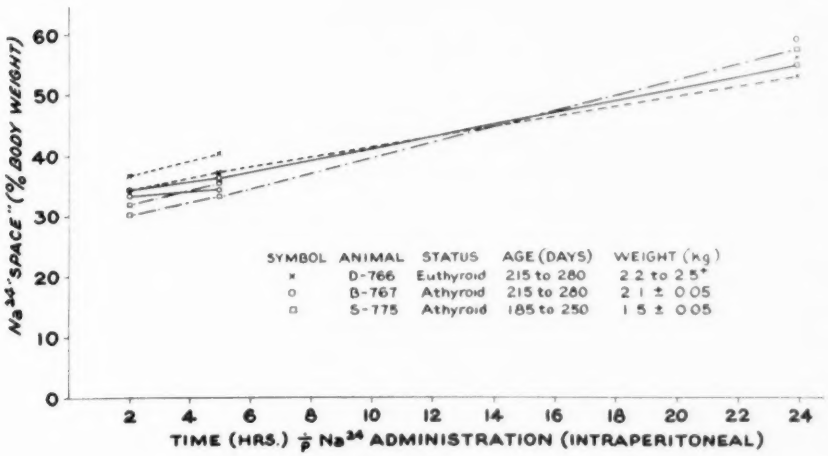
RESULTS AND COMMENT

Data are reported in two sections: (*a*) Na^{24} space in normal infant macaque monkeys during their first 150 days of life and (*b*) comparison of the Na^{24} space in normal and athyroid macaque monkeys.

During the period between 40 and 150 days of age, the volume of body fluid available for diffusion of Na^{24}, when determined 15 to 16 hours following its injection, was equivalent to 36 to 40% of body weight, demonstrating growth uniformity of the measured Na^{24} compartment (Table).

2. Bowers, J. Z., and Scott, K. G.: Distribution and Excretion of Electrolytes After Acute Whole-Body Irradiation Injury: Studies with Radiosodium, Proc. Soc. Exper. Biol. & Med. **78**:648, 1951.

Growth in these animals over the same period, as reflected by body weight gain, was uniform and declined from a rate of 10 gm. per kilogram of body weight per day at 40 days to 5 gm. per kilogram per day at 140 days, while nitrogen retention was consistently 100 ± 4 mg. per gram of body weight gain.[1a] We have found endogenous creatinine excretion to be constant (20 ± 5 mg. per kilogram of body weight per day) over the same period. The coincident uniformity in increment of Na^{24} space in the aforementioned studies was considered to reflect generally proportioned growth during the period studied. It is interesting to note that the Na^{24} space determined on animal S-755 at 18 days of age was equivalent to 47% of body weight and was significantly greater than the 36 to 40% common to all animals after 40 days. Similarly, the Na^{24} space in the human infant is described as being significantly greater than that of older children or adults.[3]



Time effect on Na^{24} diffusion in normal and athyroid macaque monkeys.

The accompanying chart presents data obtained by serial 2-, 5-, and 24-hour Na^{24}-space studies in normal and athyroid animals in approximately the same age and weight range.

Prior to discussing the similarity of Na^{24} spaces among the animals studied, consideration will be given the influence of time upon Na^{24} diffusion. In all cases the Na^{24} space was equivalent to 35 ± 5% body weight when determined 2 to 5 hours following intraperitoneal administration of the isotope and consistently increased to 55 ± 3% by 24 hours. Within three hours after its intraperitoneal or intravenous administration in the rat, rabbit, dog, or man, radiosodium has been shown to become distributed in all tissues (excluding brain and bone) in the same

3. (*a*) Fellers, F. X.; Barnett, H. L.; Hare, K., and McNamara, H.: Change in Thiocyanate and Sodium ^{24} Spaces During Growth, Pediatrics **3**:622, 1949. (*b*) Forbes, G. B., and Perley, A. M.: Estimation of Total Body Sodium by Isotopic Dilution: I. Studies on Young Adults, J. Clin. Invest. **30**:558, 1951. (*c*) Forbes, G. B., and Perley, A. M.: Estimation of Total Body Sodium by Isotopic Dilution: II. Studies on Infants and Children; An Example of a Constant Differential Growth Ratio, ibid. **30**:566, 1951.

proportion as that common to total body sodium distribution.[4] The cited authors also reported a subsequent increase in volume of distribution of radiosodium after an initial period of seeming equilibrium. From the studies of Manery and Bale [4a] and Kaltreider and co-workers [4c] it appears that up to 40% of counts injected can eventually be ascribed to the skeletal system, given sufficient time for deposition. It would seem, then, that a large part of the increment in volume of distribution of injected radiosodium was due to eventual equilibrium with bone sodium. That assumption gains substantial support by the recent report of Edelman and co-workers.[5] They found that fat-free dry bone of dog and man contains approximately 220 mEq. Na per kilogram. Using the ratio of specific activity of sodium contained in any tissue to serum sodium as an index of exchange after distribution equilibrium was attained, they reported complete exchange in all tissues, except bone, by 24 hours following injection of Na^{24}. In bone, maximum exchange was about 50%. By employing Na^{22}, which has a half-life of three years, they further observed that the portion of bone sodium exchangeable was still 50% at the end of 30 days.

Except for the cited report of Edelman and co-workers,[5] little has been done to elucidate the exact nature of bone sodium (intracellular versus extracellular and organic versus inorganic). A similarly delayed exchange with the sodium contained in the central nervous system has also been described as accounting for a small portion of the delayed increase in volume of distribution.[4] Skin loss represents still another small but obvious determinant. In the macaque monkeys studied an increase in the total volume of distribution occurred between 5 and 24 hours in a manner which closely paralleled the previously discussed increase reported for other species.[6]

In addition to presentation of the effect of time on the volume of distribution of radiosodium, the accompanying Chart allows comparison of such volumes in the normal and athyroid animals studied. While clinically myxedematous, the athyroid animals' volume of distribution generally equalled that determined in the normal at any one period after administration of the isotope.

As discussed in another communication,[1c] the myxedematous animals studied encountered significant loss in body weight within a few days following institution of therapy with *l*-thyroxine. Since these athyroid animals, on a per kilogram basis, had a volume of distribution of radiosodium equal to that of the normal or treated members, myxedematous tissue must have been available for distribution of radiosodium to the same extent and at the same rate as normal tissues (exclusive of bone and brain). Similarity in the delayed increment in volume of distribution of

4. (*a*) Manery, J. F., and Bale, W. F.: The Penetration of Radioactive Sodium and Phosphorus into the Extra- and Intracellular Phases of Tissues, Am. J. Physiol. **132**:215, 1941. (*b*) Hahn, L. A.; Hevesy, G. C., and Rebbe, O. H.: Do the Potassium Ions Inside the Muscle Cells and Blood Corpuscles Exchange with Those Present in the Plasma? Biochem. J. **33**:1549, 1939. (*c*) Kaltreider, N. L.; Meneely, G. R.; Allen, J. R., and Bale, W. F.: Determination of the Volume of the Extracellular Fluid of the Body with Radioactive Sodium, J. Exper. Med. **74**:569, 1941.

5. Edelman, I. S.; James, A. H., and Moore, F. D.: The Location and the Turnover of the Sodiums of Bone, in Conference on Metabolic Interrelations: Metabolic Interrelations with Special Reference to Calcium; Transactions of the Fourth Conference; Jan. 7-8, 1952, edited by E. C. Reifenstein, Jr., New York, Josiah Macy, Jr., Foundation, 1952, p. 240.

6. Footnote 4*a* and *c*.

radiosodium in the normal and myxedematous animals further suggested that bone sodium was probably equally available with regard to quantity and rate of exchange in the two groups.

SUMMARY

The volume of body fluid available for Na^{24} distribution was studied in normal and athyroid macaque monkeys.

At any period between 40 and 150 days of age, the 15- to 16-hour Na^{24} space in normal infant macaque monkeys was consistently 36 to 40% of body weight, while in an 18-day-old animal similarly studied the Na^{24} space was 47% of body weight.

In larger animals the Na^{24} space increased with time from $35 \pm 5\%$ of body weight at 2 to 5 hours to $55 \pm 3\%$ of body weight at 24 hours. Such increment was ascribed chiefly to a slowly acquired equilibrium with bone sodium.

The Na^{24} space was equal in normal and athyroid animals at any one period and a parallel increment with time was observed in the two groups.

FOURTEEN-YEAR REPORT OF FACIAL GROWTH IN CASE OF COMPLETE ANODONTIA WITH ECTODERMAL DYSPLASIA

BERNARD G. SARNAT, M.D., D.D.S.
ALLAN G. BRODIE, D.D.S., Ph.D.
AND
W. HOWARD KUBACKI, D.D.S.
CHICAGO

THE IMPORTANCE of the deciduous and permanent teeth in the development of the face and jaws has been a much-debated question for a long time. In 1938 a child aged 1 year 9 months was referred to us because no teeth had appeared in the oral cavity. Roentgenographic examination revealed the complete absence of teeth and tooth buds. Study of serial cephalometric roentgenograms taken up to the age of 5 years 4 months revealed that craniofacial development was within the lower limits of normal and proceeding at a normal rate.[1]

The previous report (2 to 5 years) was concerned with the period of growth and eruption of the deciduous dentition and craniofacial development. The present report is concerned in addition with a 10-year followup (6 to 16 years) of craniofacial development in the same patient with complete anodontia during the period normally covering eruption of the permanent dentition. Serial cephalometric roentgenograms and photographs were taken at periodic intervals. Five complete upper and lower dentures were constructed. No other similar study has been reported.

REPORT OF A CASE

Period from 2 to 5 Years of Age.—E. Z., a white boy aged 1 year 9 months, was referred to us on May 18, 1938, because no teeth had appeared in the oral cavity.

The mother had no difficulty during pregnancy and delivered an apparently normal full-term 3,775-gm. boy. The growth and development of the child during the neonatal and infancy periods were normal. He was given a diet consisting of breast milk (until 7 months), orange juice, and cod-liver oil under the direction of the physician.

Because the child had no teeth, the mother consulted a physician when he was about 10 months of age. He assured her the teeth would appear eventually. She was again assured on this point when the boy was 1 year 6 months of age. At 1 year 9 months the patient was referred to us after a physician had taken intraoral roentgenograms and found no evidence of tooth development.

The presence of eczema and lack of hair were noticed at 3 and 6 months of age, respectively. The patient did not perspire, and it was necessary to apply cold wet packs in order to keep him cool on hot days.

From the Departments of Oral and Maxillofacial Surgery, Orthodontia, and Prosthodontia, University of Illinois College of Dentistry.

1. Brodie, A. G., and Sarnat, B. G.: Ectodermal Dysplasia (Anhidrotic Type) with Complete Anodontia: Serial Roentgenographic Cephalometric Appraisal, Am. J. Dis. Child. **64**:1046-1054, 1942.

The father and mother were of Polish descent and had no other children. Neither parent nor any relative of the parents was known to have a condition similar to that of the patient.

Physical examination revealed a well-developed and well-nourished mentally alert boy with albinoid lanugo-like hair sparsely distributed over the scalp (Fig. 1). The skin was dry and scaly. There were neither eyebrows nor eyelashes and no axillary hair. There were no pigmentary changes in the iris; the lens and the fundus of the eye were normal. The skin of the lower eyelid toward the inner canthus was hyperpigmented and strikingly wrinkled (Fig. 1). Lacrimation was observed. The bridge of the nose seemed to lack its normal prominence. On closure of the mouth the thickened lips pouted and gave the patient an aged appearance (Fig. 1). The toe and finger nails were present and normal. The remainder of the physical examination revealed no abnormalities. After a complete anthropometric examination, the patient was reported to be within the lower limit of normal.

The blood cell count and urine were normal. The Wassermann serologic reaction was negative. Examination of roentgenograms of the carpal bones taken when the patient was aged 4 years 5 months showed four and five centers of ossification in the right and left wrists,

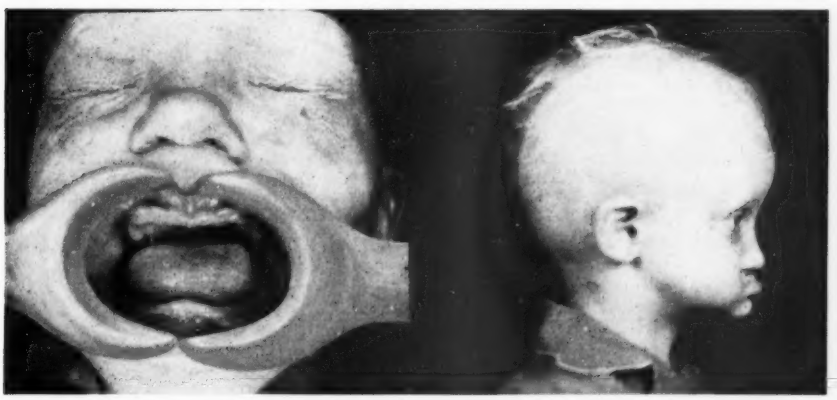


Fig. 1.—Photographs of a boy with complete anodontia and ectodermal dysplasia. Note the absence of teeth, eyebrows, and eyelashes and the pronounced wrinkling of the skin in the orbital area. In the lateral view the patient has the appearance of an aged edentulous individual. Note the sparse distribution of the lanugo-like hair.

respectively. Thus, carpal development was consistent with chronologic age. Microscopic examination of serial sections of skin obtained for biopsy from the right forearm failed to show the presence of sweat or sebaceous glands or of hair follicles. A psychometric examination (revised Stanford-Binet, Form L) at a chronologic age of 3 years and 11 months revealed a mental age of 5 years and an intelligence quotient of 128.

Period from 6 to 16 Years of Age.—During this period nothing unusually different occurred. General growth and development seemed to be well within the normal range. The albinoid lanugo-like hair of the scalp was longer and less sparse (Fig. 2). Fine short sparse eyelashes were now present. There was no evidence of eyebrows or general body hair. Four to five short brown hairs were seen in each axilla and the pubic region. The skin was still dry and scaly, and a diagnosis of atopic dermatitis was made. Slight perspiration had been observed only in the axillae. There were no siblings.

Gross Study of Increase in Size of the Jaws.—On June 15, 1942, when the patient was not yet 6 years of age, he was referred to the Department of Prosthodontia for the construction of full upper and lower dentures in order to improve masticatory function and facial appearance (Fig. 2).

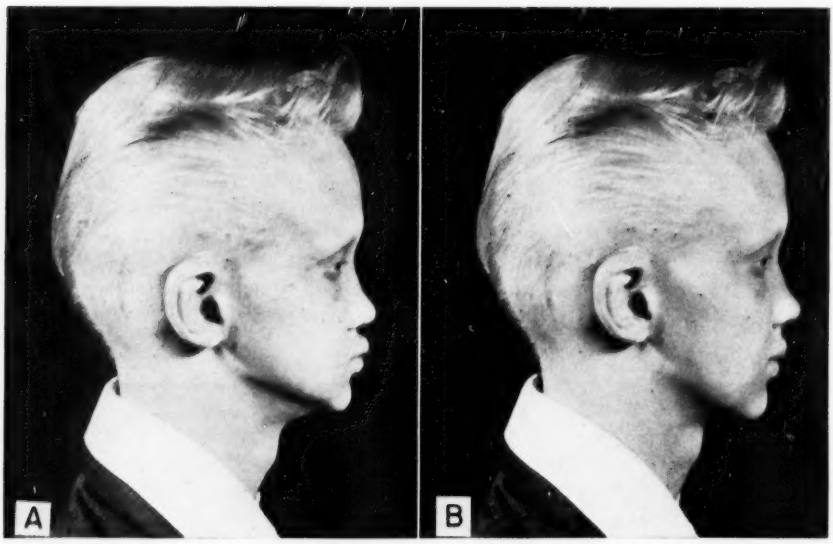


Fig. 2.—Profile photographs of same patient at 12 years of age. *A*, without full upper and lower dentures. *B*, with dentures. Note the increased amount of lanugo-like hair (See Fig. 1).

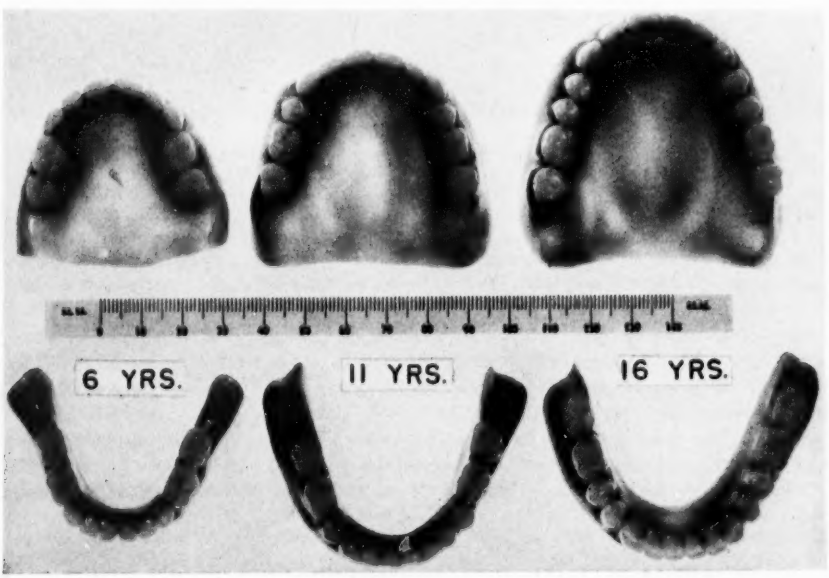


Fig. 3.—Three of five sets of full upper and lower dentures made during the period of 6 to 16 years of age. Note the increase in size of the dentures as well as the increase in the size and number of teeth.

Examination revealed a facial form and expression typical of an edentulous patient, with a loss of vertical dimension and protrusion of the lower jaw when the mouth was completely closed (Fig. 1). Intraoral examination revealed the complete absence of teeth (Fig. 1). The vestibule and the palate were well defined. There was no semblance of an upper or lower dental ridge other than a series of folds of soft movable tissue.

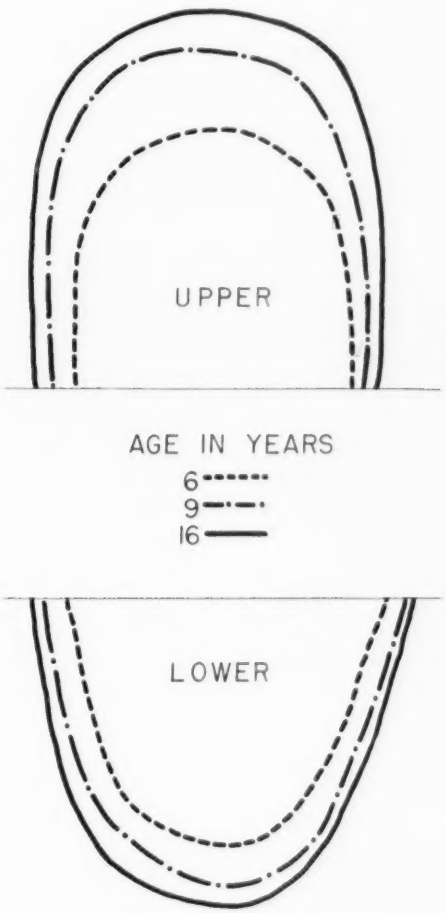


Fig. 4.—Superposed tracings of upper and lower dental arch form at 6, 9, and 16 years of age. Note increase of width and length.

Complete upper and lower dentures were constructed according to the usual methods. The jaw relationship was determined, and the proper vertical dimension and free-way space were established. A total of 20 porcelain teeth were used in the upper and lower dentures. The full complement of posterior teeth was not supplied because of the shortness of the arches (Fig. 3). The patient, despite his age, proved to be very cooperative. He learned to wear his dentures in a few days. In fact, after two days the patient had eaten popcorn for the first time in his life. The fact that he now had teeth was of tremendous value psychologically in his relations with other children.

A second set of dentures was made less than three years later because the first was too small for the upper and lower jaws. More (total of 24) and larger teeth were used, and the size of the denture was increased. A third set of dentures was constructed in July, 1947 (Fig. 3). At one time, because the upper denture had been fractured, the patient refused to go to school until the denture had been repaired. A fifth set of dentures was made in July, 1952, with a total of 28 teeth (Fig. 3). Note the increase in size of the dentures (Fig. 3) and arches (Fig. 4) with age. The dentures had little, if any, restraining effect upon the growth of the jaws.

Serial Cephalometric Roentgenographic Study.—Cephalometric roentgenograms were taken at 6- to 12-month intervals from 22 months to 16 years of age (Fig. 5). In the 1942 report the head roentgenograms of the patient taken from 1 year 10 months to 5 years 4 months were compared with the records of 20 normal white males studied during a comparable period of growth.[2] The maximum, minimum, and mean measurements of the most significant linear and angular dimensions of this control group, together with those of the patient, were given in tables.[1] These revealed that most linear dimensions fell within the range of the small normal, while angular values tended toward the mean of the control group.

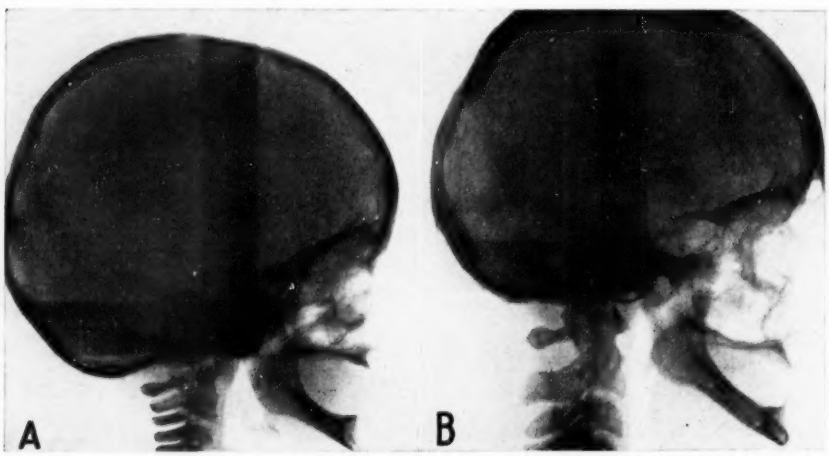


Fig. 5.—Lateral cephalometric roentgenograms of same patient with complete anodontia. *A*, at 3 years of age. *B*, at 16 years of age. Note complete absence of teeth or tooth buds. Compare the lack of development of the face (*A*) and the development of the face (*B*). Also note the development of the frontal and maxillary sinuses and the ossification of the vertebrae in *B*.

For the purposes of the present report, the findings have been shown graphically in Figure 6, where three stages of the patient's craniofacial growth (5 years 5 months, 10 years 5 months, and 15 years 6 (±1) months) have been superposed and compared with like stages of a small normal. The tracings are strictly comparable as to size and are oriented on their sella-nasion planes.

While the tracings at the 5- and 10-year levels yielded measurements of total face height (nasion to gnathion) that were slightly less than the selected normal, the two had become identical at the 15-year level. However, the nasal height, when measured from nasion to anterior nasal spine showed a progressive loss on the part of the patient from proportions (to total facial height) that were almost equal at the earlier age. When measurements of nasal height were made from the roof to the floor of that cavity, this picture was completely reversed, the

2. Brodie and Sarnat.[1] Brodie, A. G.: On the Growth Pattern of the Human Head, from the Third Month to the Eighth Year of Life, Am. J. Anat. **68**:209-262, 1941.

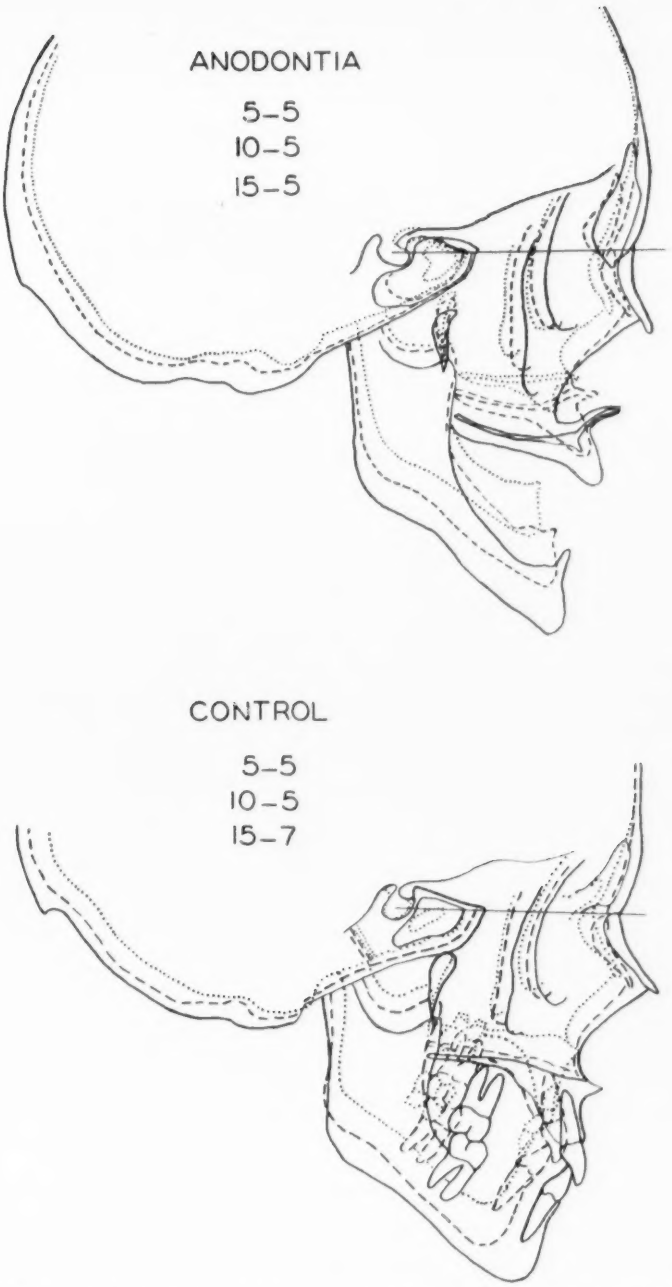


Fig. 6.—Superposed tracings of cephalometric roentgenograms at comparable ages of normal control with teeth and patient with complete anodontia at 5 years 5 months, 10 years 5 months, and 15 years 6 (± 1) months of age. Generally facial growth of the patient with complete anodontia has proceeded during this period within the lower range of normal.

patient showing excessive height over the control at the 15-year level. Comparison of the patient's tracings with those of the normal control revealed no sign of the saddle-nose that has been thought to be characteristic in these cases.

One of the most striking features observed from the roentgenograms of the patient was the extremely fragile appearance of the facial skeleton and the very high degree of pneumatization.

Fig. 7.—Photographs of two patients with complete anodontia and ectodermal dysplasia taken at approximately the same age. Note the similarity in appearance. No direct relationship between the two patients could be established. *A*, E. Z., patient in this report. *B*, E. S., patient in additional case who did not resemble his siblings.

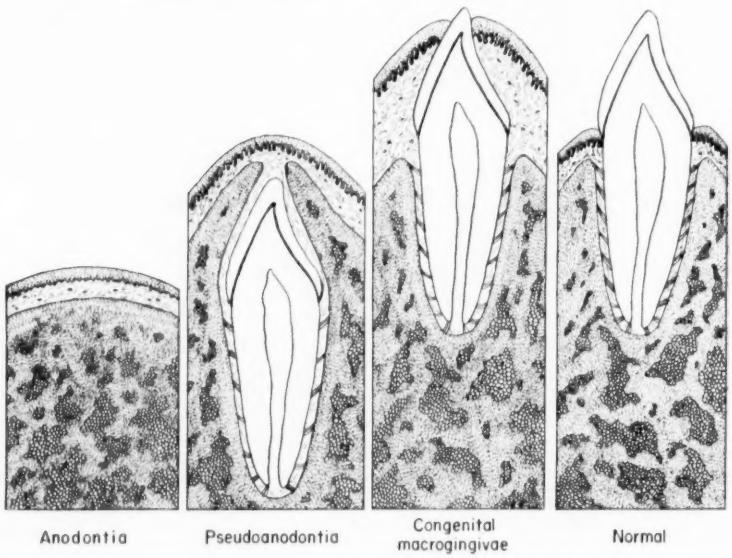


Fig. 8.—Diagrammatic representation of the differential diagnosis of the apparently edentulous child. Note in anodontia the absence of the tooth and its supporting structures, in pseudoanodontia the presence of the supporting structures and the tooth which lacked adequate eruptive force to appear in the oral cavity, and in congenital macrogingivae the presence of the tooth in its normally erupted position but covered by the markedly thickened gingivae.

All sinuses were extensive and were contained within extremely thin walls. The nasal cavity was developed far beyond the normal range except at its anterior apertures. No alveolar process was present. With these exceptions, the dimensions of the head, i. e., cranium, cranial base, depth of face, and length of mandible, were all equal to or greater than small normal.

Additional Similar Case.—In June, 1949, a second patient (E. S.), 26 months of age, with ectodermal dysplasia and complete anodontia was referred to us, and a similar study has been conducted. A set of full upper and lower dentures was supplied at 3½ years of age. It is interesting to note the striking resemblance (Fig. 7). As far as can be determined these patients are not directly related. The first patient, E. Z., has no siblings. The second patient, E. S., is the oldest of three siblings. The other two are normal.

Differential Diagnosis of the Child's Edentulous Mouth.—When a child is seen who has had no teeth appear in the oral cavity, several conditions should be considered (Fig. 8). Dental or lateral jaw roentgenograms will determine the presence or absence of tooth buds or teeth. In anodontia, because of a lack of initiation of tooth development, neither tooth buds nor teeth will be seen in the roentgenograms. If, however, unerupted teeth are seen in the roentgenograms, pseudoanodontia should be considered. Although teeth fail to erupt for various reasons, not all of them are known. In cleidocranial dystrophy the permanent teeth may fail to erupt because of ankylosis. Experimentally, eruption is retarded in hypophysectomized animals,[3] during hibernation [4] and after removal of the mandibular condyle.[5] A third condition in which a child may be seen with no teeth in the mouth is congenital macrogingivae.[6] In this instance the teeth have grown, calcified, and erupted into normal position, but because of the gingival overgrowth the teeth have been covered.

SUMMARY AND CONCLUSIONS

A patient with complete anodontia and ectodermal dysplasia has been studied clinically and roentgenographically from 2 to 16 years of age. Because of lack of sweat and sebaceous glands, he has been uncomfortable at times. The sparse lanugo-like hair has increased in amount, but still lacks pigment. Five sets of full upper and lower dentures have been designed, constructed, and delivered during this time. Each successive denture was larger and contained more and larger teeth to accommodate the increase in the size of the jaws.

Serial roentgenographic appraisal of craniofacial development during childhood and adolescence revealed the patient's over-all measurements to be at least equal to small normal. A slightly less than normal nasion to anterior nasal spine dimension coupled with a markedly greater than normal vertical measurement within the nasal cavity proper gave the impression of a buckling of the palate that is typical of a variety of facial growth arrests. This appearance was found to be due, however, to an overexpansion of the nasal cavity which was shared by its accessory sinuses. Whether this is symptomatic of this type of dysplasia or is traceable to a general weakening of the facial skeleton induced by the lack of normal dental function is a question that must await further investigation.

3. Schour, I., and van Dyke, H. B.: Effect of Replacement Therapy on Eruption of Incisor of Hypophysectomized Rat, Proc. Soc. Exper. Biol. & Med. **29**:378-382, 1932.

4. Sarnat, B. G., and Hook, W. E.: Effects of Hibernation on Tooth Development, Anat. Rec. **83**:471-493, 1942.

5. Sarnat, B. G., and Engel, M. B.: A Serial Study of Mandibular Growth After Removal of the Condyle in the Macaca Rhesus Monkey, Plast. & Reconstruct. Surg. **7**:364-380, 1951.

6. Byars, L. T., and Sarnat, B. G.: Congenital Macrogingivae (Fibromatosis Gingivae) and Hypertrichosis, Surgery **15**:964-970, 1944.

CONVULSIVE EFFECTS OF LIGHT STIMULATION IN CHILDREN

REGINALD G. BICKFORD, M.B.
DAVID DALY, M.D.
AND
HADDOW M. KEITH, M.D.
ROCHESTER, MINN.

FOR MANY years it has been known that convulsive disturbances can be produced as a result of stimulation by visual, auditory, tactile, or other sensory stimuli. Two patients whose attacks were precipitated by bright light were described by Gowers in 1881.[1] Other similar patients were discussed by Holmes [2] and by Radovici, Misirliou, and Gluckman.[3] The latter authors described attacks in a young man, consisting of rhythmic upward movements of the head, blinking of the eyes, and rotation of the head toward the sun's rays. Strauss [4] reported on one patient in whom illumination of either eye by a flashing light caused a convulsion. It was noted that the flashing light was associated with 3-cycle-per-second (cps) waves of high voltage in the electroencephalogram. In reporting on three light-sensitive patients, Cobb [5] drew attention to the importance of flickering light in contrast to continuous illumination as an epileptogenic agent. Walter and associates [6] introduced the strobotron light, which allowed more accurate control of frequency of flicker than had the sectored disk employed by previous workers. Their investigations emphasized the importance of frequency of flicker in the production of convulsive effects.

Gastaut, Roger, and Gastaut [7] used the stimulus of a flickering light while recording the electroencephalogram in 100 cases of epilepsy. They stated that in 4% of

From the Laboratory of Electroencephalography, Section of Physiology (Dr. Bickford), the Sections of Neurology and Psychiatry (Dr. Daly), and the Section of Pediatrics (Dr. Keith), Mayo Foundation, University of Minnesota, and Mayo Clinic.

1. Gowers, W. R.: Epilepsy and Other Chronic Convulsive Diseases: Their Causes, Symptoms and Treatment, Baltimore, William Wood & Company, 1881.

2. Holmes, G.: Epilepsy, a Cerebral Disease, Lancet **2**:554-555 (Sept. 14) 1929.

3. Radovici, A.; Misirliou, V., and Gluckman, M.: Epilepsie réflexe provoquée par excitations optiques des rayons solaires, Rev. neurol. **1**:1305-1308 (June) 1932.

4. Strauss, H.: Jacksonian Seizures of Reflex Origin, Arch. Neurol. & Psychiat. **44**:140-152 (July) 1940.

5. Cobb, S.: Photic Driving as a Cause of Clinical Seizures in Epileptic Patients, Arch. Neurol. & Psychiat. **58**:70-71 (July) 1947.

6. Walter, W. G.; Dovey, V. J., and Shipton, H.: Analysis of the Electrical Response of the Human Cortex to Photic Stimulation, Nature **158**:540-541 (Oct. 19) 1946.

7. Gastaut, H.; Roger, J., and Gastaut, Y.: Les formes expérimentales de l'épilepsie humaine: I. L'épilepsie induite par la stimulation lumineuse intermittente rythmée ou épilepsie photogénique, Rev. neurol. **80**:161-183 (March) 1948. Gastaut, H., and Gastaut, Y.: Un cas d'épilepsie photogénique pour illustrer l'activation de l'électroencéphalogramme par la stimulation lumineuse intermittente, Semaine hôp. Paris **25**:2707-2710 (Sept. 2) 1949.

their patients who had frank epilepsy and in 25% of their patients who had attacks of petit mal there was a possibility of provoking seizures by "abnormally irritating a part of the organism other than the brain."

Melin [8] has shown that sensitivity to light is not confined to adults. He reported on three children in whom seizures could be induced by stimulation with a flickering light.

The purpose in this paper is to report our observations on 27 children.

TECHNIQUE

In some of the earlier investigations of sensitivity to light the light from a photoflood bulb (GE-R2) was interrupted by means of a three-fourths-blackened sectoring disk. This was rotated by a variable speed motor at a rate which was controlled by a variable voltage transformer. The intensity of light was changed from a maximum of 1,200 foot-candles (f.-c.) by means of a variable voltage transformer. This apparatus gave an approximate sine-wave output of light. In later experiments, a strobotron flash tube was employed, the apparatus being that described by one of us (R. G. B.).[9] The strobotron gives short pulses of light of a duration of 50 μsec. and an intensity of approximately 300,000 f.-c. In spite of a great difference in the shape of the light pulse, the clinical and electroencephalographic responses to the two forms of light stimulation are similar. The strobotron method has the advantage that the apparatus is simple and the frequency is easily controlled.

Recordings were made by means of an eight-channel Grass electroencephalograph; solder-disk electrodes and scalp-to-scalp and scalp-to-ear combinations were employed. Artefacts attributable to flash discharge radiation were avoided by maintaining low electrode and ground resistance. Effects of various pure colors were tested by means of Kodak Wratten filters placed in a window in front of the strobotron light.

OBSERVATIONS

Our attention was first drawn to the condition under consideration by the case now to be reported.

CASE 1.—The patient was a boy, 7 years of age. When he was 5 years of age it had been noticed that in bright sunlight he would turn toward the light and wave his hands before his eyes, continuing this for as long as 10 minutes. He had not done this in the house, in school, on dull or cloudy days, or after sundown. He had had occasional attacks of headache and vomiting, and on at least one occasion such an attack had been accompanied by loss of consciousness lasting a half hour.

While the boy was in the examining room he voluntarily stood in the sunlight and waved his hand before his eyes. During this time he appeared unresponsive, as if he were in an attack of petit mal, but such an episode could be interrupted by speaking sharply to him. It was noted that these attacks could be induced by bright artificial light and that the patient was able to reproduce his attacks at will, apparently with considerable pleasure.

General physical and neurological examinations, routine studies of the blood and urine, and roentgenograms of the head and thorax showed nothing significant. By the Stanford-Binet test the boy's intelligence quotient was 85.

Originally, the nature of the episodes of hand waving was not understood. It was felt that they represented either an atypical seizure or a bizarre habit spasm of psychogenic origin.

8. Melin, K. A.: Photic Stimulation as an Aid in Electroencephalography: A Report of 3 Cases, Acta paediat. **39**:148-157, 1950.

9. Bickford, R. G., and Moffet, W. T.: A Simple Photostimulator, Electroencephalog. & Clin. Neurophysiol. **3**:251-252 (May) 1951.

Only a brief summary of the electroencephalographic studies will be made here. The pattern of the electroencephalogram with the patient resting varied widely over a period of five years in which recordings were made on this patient. At times classical 3-per-second spike-waves were seen. At other times focal slow spikes were noted and, while these appeared consistently in the tracing from one area at a given time, they were seen to shift over the years, appearing alternately in the tracings from the right occipital, left occipital, or right sylvian region. The patient was markedly sensitive to flickering light, and attacks of petit mal could be induced by photic stimulation. It was also observed that if the patient were placed before a source of bright light he would wave his hand close to his face with the fingers widely separated. This maneuver was associated with the appearance in his electroencephalogram of seizure patterns occurring synchronously in tracings from all cortical areas (Chart 1) and associated clinically with an attack consisting of arrest of speech and turning of the eyes to the left. During the attack, the patient, if allowed to continue waving his hand, would become increasingly confused and would remain so after he had spontaneously terminated the attack. If waving of he hand

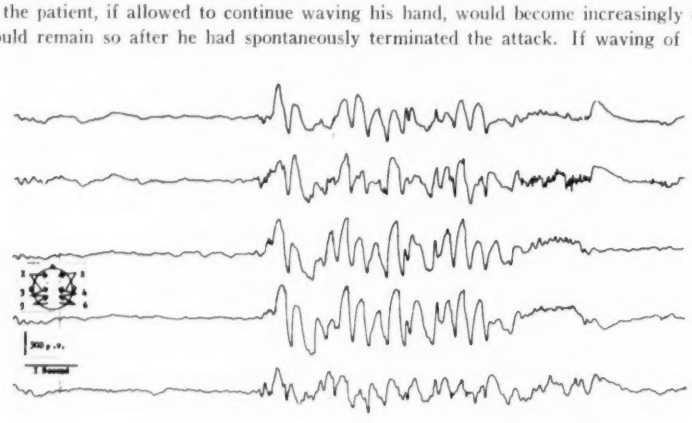


Chart 1 (Case 1).—Self-induced seizure. Patient was asked to wave his hand in front of a bright light. Hand movements were recorded by the photocell and are shown in the bottom tracing. The seizure discharge was associated with turning of the eyes and unresponsiveness.

was interrupted by another person, the patient would become resentful. However, he could be made to terminate the attack himself by someone speaking sharply to him.

A program of treatment, including administration of diphenylhydantoin (Dilantin) and phenobarbital, was prescribed. The boy was given dark glasses to wear and, with this regimen, there was temporary improvement. It was subsequently necessary to discontinue administration of diphenylhydantoin because of the development of a rash. Following this, waving of the hand became more frequent and more prolonged, although the child had no actual convulsions. Since it had been shown in the laboratory that administration of amobarbital (Amytal) sodium raised his threshold of sensitivity to light, this drug was given by mouth in doses of ½ grain (0.032 gm.) twice daily. This resulted in some improvement. Administration, also by mouth, of 5 grains (0.3 gm.) of trimethadione (Tridione) four times daily was ineffective. Both phenacemide (Phenurone) and phethenylate (Thiantoin) sodium were administered by mouth, but their use was discontinued because of skin reactions. Finally, the boy was fitted with a special pair of darkly tinted welder's goggles with side protectors which he was to wear whenever in bright light. Following this, waving of the hand has not been observed by his parents.

Case 2.—The patient was a girl 9 years old. At 6 years of age she had fallen on the street, striking her head. She had been dizzy and confused for 10 minutes. Six weeks later she had

begun to have typical attacks of petit mal. At first they had occurred only five to six times daily, but, by the time she was seen at the Mayo Clinic, they were occurring as often as 100 times daily.

General physical and neurological examination revealed nothing significant. In the course of examination, however, the patient had two petit-mal seizures, each of a duration of approximately two seconds. Results of routine studies of the blood and urine were within normal limits. According to the roentgenograms, the head and thorax were normal.

In the resting electroencephalogram were two bursts of classical 3-per-second spike-waves. Photic stimulation was carried out by use of the strobotron light. Responses to light were not seen at frequencies of less than 15 flashes per second. At 20 flashes per second a complex response, consisting of a mixture of slow waves, having frequencies of 3 and 6 cps., appeared in recordings from the posterior regions of the head. Often this slow-wave response would

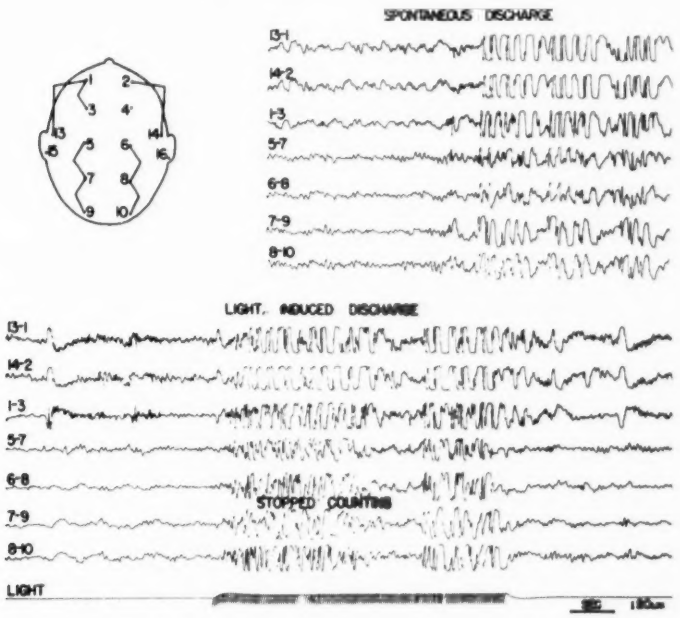


Chart 2 (Case 2).—Comparison of electrical characteristics of spontaneous and light-induced seizure discharge.

abruptly assume a spike-wave form (Chart 2) and would spread rapidly to the frontal region. These episodes invariably were accompanied by clinical attacks of petit mal.

Initial treatment was with ¼ grain (0.016 gm.) of amobarbital sodium three times daily and 1 fluidram (4 cc.) of diphenhydramine (Elixir of Benadryl) hydrochloride three times daily. On this regimen the child continued to have attacks of petit mal. She was then given 0.5 gm. of phenacemide three times daily. The attacks stopped completely for one week and then recurred. The dose of phenacemide was then increased to 0.5 gm. four times daily, and the attacks ceased. Three months later the girl remained free of seizures.

CASE 3.—An unusual case is that of a boy, 6 years of age, who had had frequent "staring spells" and three major convulsions. These symptoms had begun in the course of convalescence from a vague illness diagnosed as rheumatic fever in July, 1950. He had been confined to bed during the months of July, August, and September. The staring spells first had been noted when he had become ambulatory after this illness. It had been noted that the boy would stare

fixedly at the screen or the window curtain and would blink and be unresponsive. The parents felt that the spells also had been produced by the boy's staring at cloth of a fine pattern. The first generalized convulsions had occurred late in September, while the boy was staring at a loose-textured curtain. Two further generalized seizures had occurred in November of the same year. During this period the staring spells had become more frequent than before. The boy often surreptitiously would gaze at his father's coat and would be seen to have an attack of petit mal.

On physical examination the blood pressure was 105 mm. of mercury systolic and 65 diastolic. A very soft variable systolic murmur was heard at the apex of the heart. The remainder of the physical and neurological examination showed nothing significant.

The concentration of hemoglobin and the number of leucocytes in the blood was normal. The sedimentation rate was 10 mm. per hour (Westergren method). The electrocardiogram was normal. Roentgenograms of the head and thorax did not disclose any abnormality.

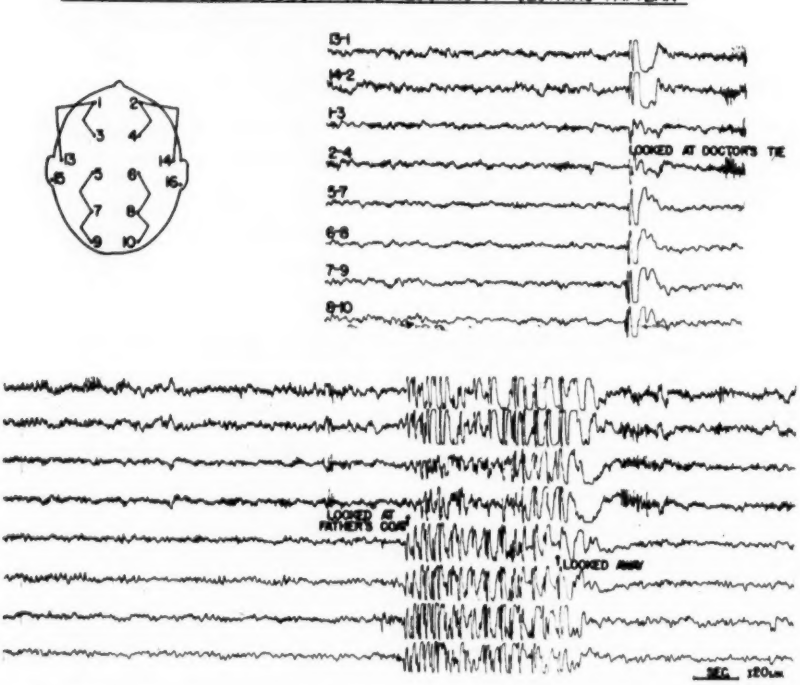


Chart 3 (Case 3).—Seizure discharges produced by looking at a necktie (above) and the pattern of a coat (below). Intermittent rolling of the eyes occurred during the seizure discharge.

In the electoencephalogram, with the patient resting, were intermittent sharp waves, derived from both occipital areas. On rare occasions a typical 3-per-second spike-wave burst appeared in tracings from posterior regions of the head, and at times the abnormal discharges occurred synchronously over the entire cortex. It was noted that any startling stimulus, such as a hand clap or a single flash of light, often would evoke a single spike-wave. When the strobotron light was used, there was no evidence of abnormal discharge until the rate of flicker reached 15 flashes per second, at which time long-sustained bursts of classical spike-waves, associated with clinical attacks of petit mal, were seen. Measurement of the light intensity threshold indicated that even the dimmest flickering light (30 f.-c.) at the proper frequency was sufficient to produce an attack. Studies of sensitivity to patterns showed that when the child looked at a finely woven cloth, such as his father's corduroy jacket (Chart 3) or the fine weave of a poplin storm coat, there would be a burst of spike-waves associated with a clinical attack of petit mal; this

*Summary of Cases**

Case	History and General Examination: Age, Yr.	Sensitivity to Light	Type of Attacks	Characteristics of Electroencephalogram and Observations in Electroencephalographic Laboratory: Resting EEG	Type of Discharge Produced by Light	Effect of Stimulation by Light	Effect of Anticonvulsant Drug
10	2	No	G. M.; mental retardation; I. Q., 49	S. W.	S. W.	Myoclonic jerks	.....
11	11	Yes	G. M.; P. M.	Rare S. W.; normal background	Multiple spike and wave	Eye turning to left or right and rotation of eyes; arrest of counting	.....
12	12	No	Typical G. M. at irregular intervals for 4 yr.	3/sec. S. W.'s; increase with eyes closed	S. W.	Eye turning to right	Trimethadione suppressed attacks
13	13	No	Headaches; no epilepsy; lesion left basal ganglion region by pneumoencephalogram	Dys. II; increase with eyes closed	Atypical S. W.	Dizziness	.....
14	4 3/12	Yes	Irregular general seizures; "falling"; gross tremors of extremities; ataxia	Multiple spike and wave	Spike	Myoclonic jerks of eyelids	.....
15	9	No	P. M. for 6 mo. at 3½ yr.; started G. M. at 7 yr.	Dys. II (fast)	Multiple S. W.	None	.....
16	13	No	P. M. 2 yr.	S. W.; increase with eyes closed	Atypical S. W.	None	.....
17	4 10/12	...	Minor G. M. 3 weeks; P. M.	Focal sharp wave from occip.	Atypical S. W.	None	.....
18	4	...	Cerebral degenerative disorder; G. M. attacks; mental retardation; I. Q., 32	Slow S. W.	Sharp wave with single flash; multiple S. W. with fast rates	Myoclonic jerking with single and multiple flashes	.....
19	10	No	P. M. for 10 mo.	S. W.; increase with eyes closed	S. W.	Myoclonic face twitching	Trimethadione abolished spontaneous disorder and reduced disorder caused by light
20	4	?	Mental retardation; I. Q., 35; no convulsive disorder	Dys. II	Multiple S. W.	Myoclonic jerks of eyelid, head, and upper limbs	.....
21	9	No	G. M. 8 yr.; I. Q., 69+	S. W.; increase with eyes closed	S. W.	None	.....
22	11	Yes	Mental retardation; I. Q., 31; convulsive disorder; G. M. and P. M.; since 8 mo. old	S. W.	S. W. on single flash and multiple S. W.'s at fast rates	Myoclonic jerking	.....
23	9 9/12	No	P. M. for 3 yr.	Normal	Atypical spike disorder	None	.....
24	13	No	G. M. for 2 yr.	S. W.	S. W.	Head and eyes to left; speech arrest	Trimethadione suppressed attacks
25	1 8/12	No	P. M. for 10 mo.	Multiple S. W.	Atypical S. W.	"Jerking"	.....
26	10	No	Mental retardation; I. Q., 62	S. W.; increase with eyes closed	Multiple S. W.	Speech arrest; head and eye turning to left	.....
27	3	No	Mental retardation; I. Q. under 20; severe flexor spasms; myotonic	Right occipito-parietal sharp wave focus	Atypical S. W.; accentuation of sharp wave dis.	None	.....

* G. M. indicates grand mal. S. W. indicates spike-wave. P. M. indicates petit mal. Dys. II indicates nonspecific rhythmic discharge.

attack could be terminated by commanding the patient to look away or by reducing the intensity of the illumination on the pattern. Fine copper mesh also was shown to be an extremely effective stimulus and long-sustained episodes of spike-waves, associated with difficulty in speaking and mental confusion, occurred when the patient looked at such mesh.

The program of treatment included administration of phenacemide and the wearing of dark sun glasses. This resulted in definite reduction in the frequency of seizures.

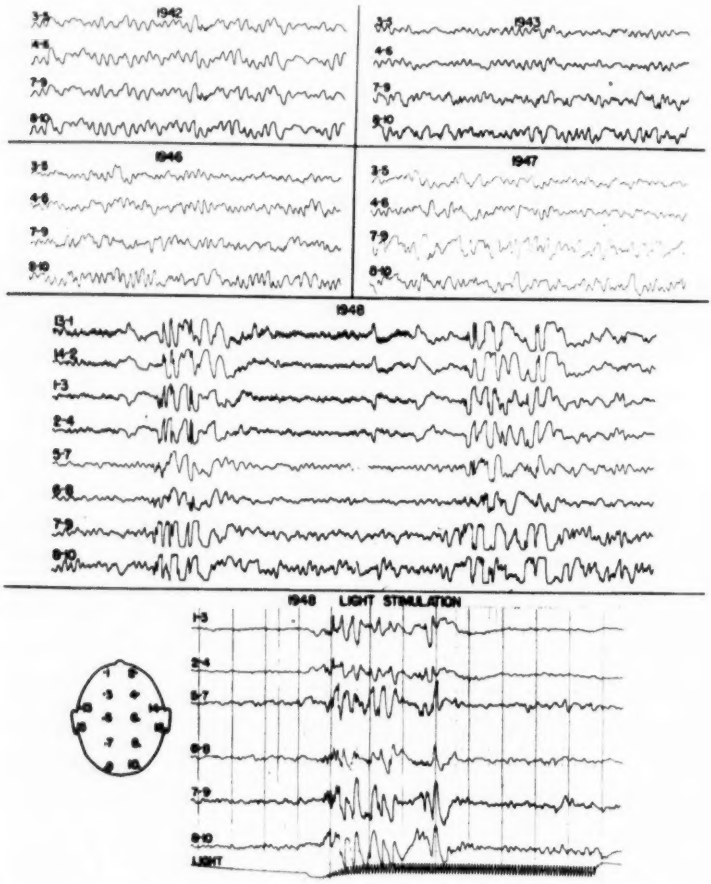


Chart 4 (Case 4).—Serial electroencephalograms made over a period of eight years, showing the development of a spike-wave discharge, with sensitivity to light, in a child who had been free from major and minor seizures since 1942.

Sensitivity to light has been of importance in the clinical management of 24 other patients, while in the management of still others it has been largely of academic interest. Abstracts of the findings relative to some of these patients are given below, and the remainder are briefly described in the Table.

Case 4.—A girl, 2 years of age, had begun to have convulsions at the age of 7 months. They had occurred about once a month, had been generalized, and had been characterized by loss of consciousness, biting of the tongue, and cyanosis. Usually they had been followed by deep sleep. There had been no birth injury, and nothing significant was found on general examination.

The electroencephalogram was studied over a period of 6 years (Chart 4). The record taken in 1942, when the patient was 2 years old, gave evidence of a diffuse, nonspecific type of dysrhythmia of moderate voltage. Most of the abnormal waves were in the range of frequency of 4 to 7 per second. A recording made a year later, in 1943, gave evidence of some improvement and was considered to be within normal limits for a child of 3 years. At this time the girl had been free of seizures since the last recording, when administration of diphenylhydantoin and phenobarbital had been started. In a third recording, made in 1946, the abnormality was increased, and some diffuse synchronous atypical spike-waves appeared maximally in recordings from the occipital areas. In a recording made in 1947 were rhythmic 3- to 6-per-second waves of high voltage occurring in long trains. These appeared on the patient's closing her eyes and were maximal in recordings from the occipital areas. In 1948, when the patient was receiving full medication, and at a time when she had been free from seizures since 1942, further deterioration was evident in the resting record with the appearance of fairly well organized synchronous high-voltage spike-waves. There was a marked tendency for these spike-waves to occur with closing of the eyes. At the end of this recording the girl was subjected to flicker stimulation for the first time and was found to be markedly sensitive to light. Light flickering at rates of more than 5 per second induced diffuse bilaterally synchronous spike-waves. Some of these discharges were accompanied by myoclonic jerking.

Remarkable features of the recordings made on this patient were the progressive deterioration which occurred in the electroencephalogram, with the appearance of spike-waves and the development of sensitivity to light at a time when medication had entirely prevented any convulsive seizures. This presumably indicates that the medication in this case was acting at some location peripheral to the origin of the abnormal discharges.

Case 5.—For two years before a boy attained the age of 11 years it had been noted that he had recurrent episodes of blinking his eyelids. At one time these episodes had been associated with an attack of mumps. Two months before his admission he had had two generalized convulsions not associated with fever or illness. On physical examination abnormalities were not found. The intelligence quotient (Wechsler-Bellevue) full scale was 89. The only abnormal laboratory finding was in the electroencephalogram. A recording in June, 1947, showed high voltage sharp-wave discharges of maximal amplitude in the occipital areas bilaterally and slightly more marked on the left side. These discharges were completely inhibited by the patient's opening his eyes. Light stimulation delivered by means of a sectored disk at a frequency of more than 12 flashes per second produced high-voltage synchronous spikes and spike-waves; the former were maximal in recordings from the motor areas, and the latter were maximal in recordings from more posterior areas. These discharges were associated with clinical attacks characterized by opening of the eyes, staring, and arrest of speech, followed by conjugate deviation of the eyes to the right. A total of 35 separate attacks of this type were induced, and it was notable that the boy seemed unaware of their occurrence. A year later, in June, 1948, the resting record was essentially the same as was a further recording made again a year later, in 1949. Unfortunately, further studies of the effect of light were not made in the course of either of these recordings.

Case 6.—The patient was a girl, aged 10 years. When she was one year of age, she had had a series of brief attacks of interruption of consciousness, without other clinical features. Treatment for infestation with whipworm had been given, and the attacks had ceased. At the age of 4½ years, following otitis media, the attacks of petit mal had recurred. The mother noticed that these attacks had been aggravated by exposure of the patient to bright sunshine. At 9 years of age the girl had her first generalized convulsion.

Physical examination revealed nothing significant and, except for the electroencephalogram, laboratory studies did not contribute anything of value. A feature of the resting record was the occurrence of multiple spike-waves related to the patient's closing of her eyes. These discharges were maximal in recordings from the occipital areas, or they were confined to recordings from these areas. With stimulation by light, delivered with the sectored disk, marked activation of the recording occurred, with diffuse discharges consisting of multiple spike-waves representing the whole cortex. These frequently occurred in short bursts, with relatively little intervening background activity. During stimulation with light at 12 flashes per second it was noted that the

girl's head turned to the left, and this was followed, in a second or two, by flattening of the record of all areas. There was then a build-up of fast activity commencing in the recording from the right occipital area and rapidly becoming generalized. This was associated with stiffening of the body and jerking. A generalized seizure developed, and diffuse discharges of high voltage were recorded in the electroencephalogram.

It is interesting that flattening of the record occurred between development of the high voltage spike-waves associated with stimulation of light and the occurrence of a generalized seizure. This apparently represents a period of transition from the mechanism of the petit mal seizure to that of the attack of grand mal.

CASE 7.—The patient was a girl, aged 13 years. At 2 years of age she had had a convulsion associated with a febrile illness. At 6 years, a second convulsion had occurred; it had been generalized, had lasted three minutes, and again had been in association with a bout of fever. Following this, about every 10 months the girl had had a generalized convulsion which always had been nocturnal and, with one exception, always had been associated with fever. During this time she had had some febrile illnesses without associated convulsions.

Physical examination revealed nothing significant, nor did laboratory examinations, except for the electroencephalogram. In the resting record were rhythmic bilaterally synchronous waves of high voltage at a frequency of 3 cps; they occurred in the occipital areas. They often occurred as a rhythmic train following closing of the patient's eyes. Occasionally these discharges on closing of the eyes were associated with some low-voltage spikes, at which times they resembled typical spike-waves. At one stage during hyperventilation there was a short burst of diffuse synchronous high-voltage rhythmic discharges at a rate of 4 cps, associated with some low-voltage spikes. No classical spike-wave discharges were seen, however, at any time during the recording. Light stimulation delivered by means of the sectored disk at frequencies up to 8 flashes per second produced an increase in the slow wave discharges from the occipital areas. With rates of stimulation of more than 10 per second, the occipital discharges became more clearly organized into rhythmic bursts; at a rate of 3 to 4 per second, these bursts frequently spread to involve the rest of the cortex. Associated with these discharges was a complaint of "dizziness."

A recording made on this patient while she was asleep contained some intermittent complexes consisting of spikes and slow wave patterns occurring diffusely and synchronously.

CASE 8.—A boy, 13 years of age, was first examined in January, 1951, because of generalized convulsions which had begun in 1946 and had recurred at intervals of from three to nine months. The onset of the convulsions usually had been heralded by a tendency to myoclonic jerking and a feeling of "jumpiness" and "nervousness." From this state, which might last minutes to hours, the boy suddenly would go into a generalized convulsion, with loss of consciousness followed by vomiting and headache. In September, 1949, his clavicle had been fractured and a roentgenogram taken of his head at that time had revealed an old fracture over the right eye. His intelligence quotient was 80 (Wechsler-Bellevue scale).

On examination, marked intention tremor with scattered myoclonic jerks was evident. His metatarsal arches were high. He resembled other patients described by Ramsey Hunt under the title, "Dysynergia Cerebellaris Myoclonica."

The resting electroencephalogram was grossly abnormal and gave evidence of numerous episodes of spike-wave discharge occurring diffusely and synchronously. They were maximal anteriorly. Sometimes isolated spikes might occur, particularly in recordings from the motor areas. There was a tendency for the spike-wave discharge to occur on the patient's closing his eyes. Light stimulation at rates in excess of 8 flashes per second caused marked increase in the abnormal discharges and the appearance of multiple spikes with associated slow waves. Occurrence of these discharges was associated with marked myoclonic jerking of the head and arrest of speech.

Intravenous injection of 0.5 gm. of trimethadione, together with 0.5 gm. of urethan, markedly reduced the amount of activity which accompanied the spontaneous seizures. The amplitude of the response to light also was reduced. There was a decrease in the amount of myoclonic jerking and arrest of speech was not observed after administration of trimethadione. The effect of medication began to decrease after about 20 minutes.

CASE 9.—The patient was a boy, 14 years of age. Two years before his admission he had had three periods of unconsciousness without convulsions. One month before his admission he had had three attacks of unconsciousness, one accompanied by turning of the head to the left and one by a generalized convulsion.

Nothing significant was found on physical examination, and the results of laboratory examinations were not unusual except for the electroencephalogram. In the resting record were two episodes of well-sychronized diffuse 3-cps spike-wave discharges. One of these episodes followed closing of the patient's eyes; the other occurred at the end of hyperventilation. In the rest of the record were only some scattered slow waves.

Stimulation by light at rates of more than 10 flashes per second, effected with the sectored disk, gave rise to diffuse, bilaterally synchronous spike-wave discharges at a rate of 3 cps. In some instances the spike components were of reduced conspicuousness, and the discharge consisted primarily of rhythmic waves of 3 cps. Arrest of speech was noted in the course of some of these discharges, but myoclonic jerking was not seen. The effect could be produced with the patient's eyes either open or closed.

Intravenous injection of 0.025 gm. of amobarbital sodium produced marked diminution of sensitivity to light and entirely suppressed seizure discharges at the highest intensity of light. This effect soon passed off, however, and the discharges began to return within five minutes. The patient noted, during the time of the maximal effect from amobarbital sodium, that the light did not appear so bright. He was advised to wear dark glasses outdoors or when exposed to any bright light.

COMMENT

Review of the cases presented suggests that three separate classes of patients with regard to sensitivity to light can be recognized. They can be described as (*a*) a clinically sensitive group in which light of the intensity encountered in daily life is capable of inducing clinical attacks; (*b*) a less sensitive group in which clinical seizures can be induced only under conditions of high intensity of illumination and rapid flicker which can be produced in the laboratory and, finally, a group (*c*) in which the only evidence of sensitivity is the occurrence of seizure discharge in relation to stimulation by light and unaccompanied by any detectable clinical evidence of seizure.

Such a classification probably indicates little more than progressive lowering of the convulsive threshold from the electrographically sensitive group to those that are clinically sensitive. Patients may sometimes shift from one group to another as a result of spontaneous change, as indicated by day-to-day testing. They may in many cases be moved from the low threshold group by means of anticonvulsant medication.

Administration of pentylenetetrazole (Metrazol) to patients of the electrographically sensitive group frequently will result in their developing clinical manifestations. A difficulty in the classification given is caused by the fact that patients of Group (*c*) may be difficult to separate from patients of Group (*b*) on the one hand and from patients who present one of the variants of the normal driving response on the other. In spite of these limitations, the classification seems to be useful, particularly as an indication to the clinician of the severity of the sensitivity to light in any particular case. On the basis of the classification, 5 of our cases fall into Group (*a*), 15 into Group (*b*), and 7 into Group (*c*).

A common complaint among these patients is that their attacks have been induced by the flickering produced by motoring through an avenue of trees when the sun is low. Other common complaints are of difficulty when looking directly at the sun or at reflecting light from snowscapes or water. Young children may manifest this by blinking and rolling of the eyes. In two cases waving of the hand when facing the sun or a bright light produced enough flickering to induce attacks. These unusual patients, who often present a large psychopathologic component, will be subjects of a separate study.

The usual clinical manifestations of sensitivity to light may be blinking, turning of the eyes, jerking of the head or arms, arrest of speech, and sometimes mental confusion or loss of consciousness. If the flickering is prolonged, a generalized seizure may occur; this happened in 2 of our 27 patients.

RESTING ELECTROENCEPHALOGRAPHIC RECORDINGS

The resting electroencephalograms of these patients do not show any pattern which is diagnostic of the condition. The most common type of abnormality is the diffuse high voltage three-per-second spike-wave discharge which about three quarters of the group displayed (Chart 4). Five patients showed focal sharp-wave discharges confined to the occipital regions. A rather frequent feature was the presence in the occipital areas of rhythmical bursts of high-voltage waves related to closing of the eyes. A perfectly normal record was obtained when one patient was at rest and the normal background of another patient was interrupted at very infrequent intervals by a spike-wave discharge.

DISCHARGE PRODUCED BY LIGHT

The usual type of discharge produced by the stimulation of flickering light was the diffuse spike-wave which might have the classical three-per-second configuration or more commonly was of a distorted atypical variety (Chart 4). In many instances, and particularly in those in which myoclonic jerking occurred, a multiple spike- and slow-wave pattern was produced. Frequently, although not invariably, these discharges were more easily induced when the eyes were closed. In two cases, spike-wave discharges could be triggered by a single flash.

EFFECTIVE FLASH FREQUENCIES

The most effective flash frequencies were found to lie between 10 and 20 flashes per second. Many patients, however, were sensitive in the range of 6 to 30 per second. In rare instances patients are sensitive to single flashes or even to light of unvarying intensity.

CLINICAL ACCOMPANIMENTS

Usually myoclonic jerking was closely related to the appearance of spike discharge in the electroencephalogram. Arrest of speech, however, which was tested by having the patient count during the period of stimulation, was of very variable relationship to the seizure discharge (Chart 4). The arrest of speech frequently occurred some seconds after the discharge had begun. Most patients were conscious during this period when speech was arrested, as is proved by their ability to recall things that had been said in this time. Others, however, did not recall remarks made, or they might give evidence of some confusion concerning events of this phase. Another observation of clinical interest is that the direction in which some patients turned the head and eyes was inconstant and might change from one direction to another in the course of repeated testing over several minutes.

MECHANISM OF CONVULSIVE EFFECTS

Perhaps the most striking feature on reviewing the electroencephalographic and clinical effects of stimulation by light is the extreme variability of, and the difficulty in making generalizations in regard to, the possible underlying mechanisms. This

may mean that a variety of mechanisms is operative and that it would be fruitless to attempt explanation in terms of a unitary system. With this in mind, the three possible pathways for the convulsive effects have been represented in Chart 5. The transcortical pathway (1) which constitutes a purely cortical extension of the convulsive response from the primary visual areas is perhaps the simplest conception. However, the usual simultaneous occurrence of the photically induced discharge in all areas of the cortex and the absence of any evidence of extension or of a convulsive process from occipital areas, with sequential involvement of the rest of the cortex, may be taken as evidence against this particular mechanism.

It will be noted that Pathways 2 and 3 of Chart 5 concern the same final common mechanism, namely, the activation of a diffuse thalamocortical system. Jasper [10] has suggested that such mechanism may be responsible for the spike-wave discharge

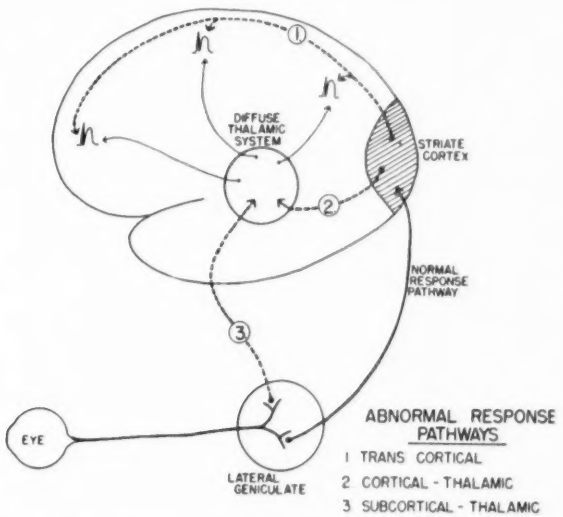


Chart 5.—Hypothetical pathways for the convulsive response to light.

of petit mal. The participation of this or of some equivalent system in genesis of the light-induced discharge seems likely in view of (1) the similarity of resting and light-induced discharges, (2) the frequent occurrence of an approximate spike-wave pattern in both the resting and the induced discharge, (3) the synchronous appearance of widespread cortical discharges, suggesting their mediation by a diffuse network, and (4) the observation that photosensitivity is usually only one facet of an established epilepsy in which frequent seizures occur in the absence of stimulation by light. This last observation would seem to require a system possessing the property of spontaneous discharge as well as the possibility of triggering under the influence of activating stimuli, such as might be brought to bear by Pathways 2 and 3.

The question remains as to whether this thalamocortical system is activated by purely subcortical pathways, as in Pathway 3, or by a pathway originating in the

10. Jasper, H. H., and Droogleever-Fortuyn, J.: Experimental Studies on the Functional Anatomy of Petit Mal Epilepsy, A. Res. Nerv. & Ment. Dis., Proc. **26**:272-298, 1947.

occipital cortex (Pathway 2). On the basis of evidence presented at this time, it is difficult to distinguish between these two pathways. Pathway 3 is the shorter anatomically and therefore the easier to conceive in terms of a pathologic short circuit. However, the rather frequent occurrence (in 25% of our cases) of focal occipital electroencephalographic abnormalities in the resting record lends some support to the thesis of a primary occipital derangement of function of the kind depicted in Pathway 3.

ANTICONVULSANT DRUGS

In seven cases the effect of intravenous anticonvulsant medication was tested in the period of stimulation by light. In one instance the effect of phenacemide given by mouth over a period of several days was observed. Any of three drugs, trimethadione (Chart 5), amobarbital sodium, or phenacemide, has been found to reduce or entirely to suppress, the various manifestations of sensitivity to light (clinical and electroencephalographic) shown by these patients (Chart 6). Frequently, however, the effect of trimethadione is short-lived, and the convulsant effect of light might again become apparent within 30 to 60 minutes of initial injection of

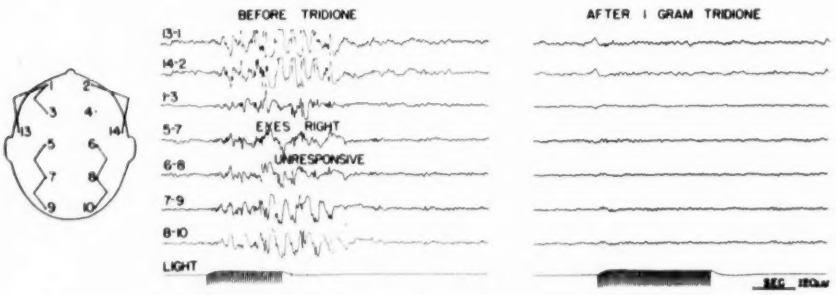


Chart 6 (Case 12).—Effect of intravenous injection of 1 gm. of trimethadione (Tridione) and 0.75 gm. urethan on the convulsive response to light. The tracing on the right was taken two minutes after completion of the injection.

the drug. Amobarbital sodium frequently has to be given in doses which produce considerable drowsiness and some ataxia in order to produce complete suppression of sensitivity to light. A further complication of these observations is the fact that the clinical effectiveness of these drugs, when given over a long period, does not always parallel their anticonvulsant effects as observed in short-term testing of this kind. Since the solution of trimethadione used for intravenous injection contained an equal quantity of urethan to aid solution, it is possible that the discrepancy in this instance may be, at least in part, attributable to an anticonvulsant property of the urethan itself. This possibility is being investigated further.

STUDIES OF FILTERS AND GLASSES

In a number of these cases an attempt was made to ascertain what part of the spectrum was responsible for the convulsive effects of light. This question is of considerable practical and theoretical interest, but unfortunately it is difficult to obtain quantitative data on it since such complex factors as spectral transmission of the source of light, transmission by the eyelids (since most marked effects are

obtained with eyes closed), transmission by the filters, and the spectral sensitivity of the eye have to be taken into consideration. Details will not be presented here, but in general it may be said, as a result of extensive observations made on four patients, that the convulsive effect of light is not confined to any small segment of the visible spectrum, since seizures may be produced with pure red, green, or blue light.

Filters.—In conformity with the findings just recounted is the fact that the patients could not be completely protected by the use of filters which excluded one color such as minus red, minus green or minus blue (with the exception of minus red with eyes closed, this combination almost completely extinguishes visible light). While the findings suggest that all parts of the visible spectrum contribute to the effect, there is an indication that in some patients the red end of the spectrum may be relatively more effective.

Glasses.—If clinical attacks occur only in relation to light (three patients in this series), use of glasses which contain a neutral filter is often a very effective therapeutic measure. The glasses must be fitted with side protection to exclude oblique light. To be completely effective, it is often necessary to reduce transmission of light to an uncomfortably low level, and in some instances welder's glasses have been used for this purpose. Since some children do not tolerate these for long periods, adjustable polaroid spectacles have been tried. By rotating one of the lenses of such spectacles, transmission of light can be adjusted to suit the prevailing conditions of illumination. In general, we have recommended deeply tinted or polaroid spectacles for patients who give evidence of having photoepilepsy and for those who are highly sensitive to light under laboratory conditions. In these cases, excellent therapeutic results have been obtained. The limiting factor almost always is the willingness of the patient to wear the glasses.

SUMMARY

Of 27 children with epilepsy who were sensitive to flickering light, some had attacks following exposure to the flickering light encountered in daily life. Others gave clinical or electroencephalographic epileptic responses to flickering light which could be produced under laboratory conditions only. There is no electroencephalographic pattern which is diagnostic of this condition.

Myoclonic jerking was found to be closely related to the appearance of spike discharges in the electroencephalogram. Arrest of speech was in a variable relationship to the appearance of spike discharges. Turning of head and eyes also was inconstant and might change from one direction to another. The most effective flash frequencies were found to be between 10 and 20 per second. The lower limit was 1 flash per second, the maximal frequency investigated was 35 flashes per second. Certain anticonvulsant drugs when given intravenously could suppress or reduce the manifestations of sensitivity to flickering light, but the effect was brief. It did not necessarily parallel the anticonvulsant effect when the drug was given by mouth over an extended time. For certain patients, whose clinical attacks occurred in relation to flickering light, the wearing of darkly tinted or polaroid spectacles has been effective in preventing attacks.

SURGICAL TREATMENT OF INTUSSUSCEPTION IN INFANTS

Effect of Added Appendectomy

HARRY M. RICHTER Jr., M.D.
AND
JEROME M. SILVER, M.D.
CHICAGO

THE EFFECT of appendectomy in the course of the surgical treatment of intussusception has deserved review in the light of recent experience. Since no report concerning this subject has appeared since 1945, when antibiotics became available for general clinical use, the following statistical analysis has been made of data from the Michael Reese Hospital records of all intussusceptions in infancy and early childhood for the period from 1946 through 1951.

Appendectomy in these circumstances is occasionally necessary to remove a necrotic or infarcted organ. It has been proposed as a method of preventing recurrent intussusception. It has also been performed for prophylaxis against future appendicitis and to obviate misleading implications of a right lower quadrant surgical scar.

Preoperative Condition of Patients

	Rectal Temperature, F.		Age, Mo.		Duration, Hr.	
	Average	Range	Average	Range	Average	Range
Simple surgical reduction.....	99.90	98-102.6	9.2	2-24	24.6	5-65
Reduction and appendectomy.....	99.95	98-102	10.7	4-24	29.1	6-146

Appendectomy after surgical reduction has often been condemned as being far too dangerous to employ routinely. An edematous inverted appendical stump has been reported as the leading point for recurrence of intussusception.

In many excellent surveys of large series which have appeared every year in the literature, the mortality, with and without appendectomy, has often been tabulated. With no ancillary data recorded, the authors and readers alike have been reduced to speculation that the greater mortality in some series was the result of the additional procedure, or that the lower mortality in others was the result of selection of less seriously ill subjects for additional appendectomy.

MATERIAL AND METHOD

In our material there have been 48 patients and no deaths. Morbidity has been measured as the number of days, surgical and after, on which the postreduction rectal temperatures had reached or exceeded 101 F. Comparison of preoperative rectal temperatures and durations of symptoms prior to reduction showed our groups of patients to be essentially identical in preoperative condition (Table). However, the group with added appendectomy averaged somewhat

Department of Surgery, Northwestern University Medical School and Michael Reese Hospital (Dr. Richter); Resident in Surgery, Michael Reese Hospital (Dr. Silver).

older than the group on whom simple surgical reduction was performed. To avoid comparison of unlike groups, all cases of patients over 24 months of age were dropped, leaving the two surgical groups practically identical with respect to age. Four patients had associated ileoileal intussusception, and two had pure ileoileal disease. None of these had appendectomy; they represent the only apparent selection in this study, although their preoperative status was similar to that of the other patients. One Meckel's diverticulum was found proximal to the intussusception and was not removed in the simple surgical reduction series.

Most of the patients received penicillin, a few, other antibiotics and small amounts of blood and plasma. There was one recurrence, five months delayed, in a patient whose appendix had been removed.

The surgical pathologist reported one specimen as a gangrenous appendix, several as organs with hemorrhagic appendicitis or acute periappendicitis, and others as dilated or normal organs. Several of these specimens were considered by the surgeon to be infarcted and their removal mandatory. From one ileoileal intussusception 1 cm. of infarcted tissue was resected.

RESULTS

The morbidity after simple surgical reduction in 19 cases averaged 2.1 days (range, 0 to 6 days) in which fever of 101 F. or higher was reached. When appendectomy was added, in 15 cases, in a group of patients otherwise nearly identical, the morbidity averaged 3.0 days (range, 0 to 6). There were no deaths or other complications which could be analyzed as further clues to measurement of the "surgical load" of added appendectomy. Statistical comparison by the method of pooled variances reveals no significant difference between these groups.

Reduction by barium enema in seven cases was followed by temperature of 101 F. for one day in only one patient. Three patients in their third year were included in this small group.

COMMENT

The additional maneuver of appendectomy performed at the time of surgical reduction of intussusception in infants seems to add little morbidity when antibiotics are used in the postoperative regimen.

Case Reports

ENDOCARDIAL FIBROELASTOSIS

Report of Unusual Case with Impaired Ability to Fabricate Serum Proteins

BEN E. KATZ, M.D.
MINNEAPOLIS
AND
FORREST H. ADAMS, M.D.
LOS ANGELES

ENDOCARDIAL fibroelastosis or endocardial sclerosis until recently has been looked upon as a pathologic diagnosis.[1] With the growing interest in this condition, attempts have been made to define this as a clinical entity and one which in many cases can be diagnosed ante mortem.[2]

The postmortem findings of endocardial fibroelastosis have been described in infants from 3 days to 5 years of age; the majority of the deaths have been of infants between 4 and 9 months. Generally speaking, three clinical patterns have been noted, characterized best by their course: (1) sudden death occurring 24 to 48 hours after the onset of symptoms of respiratory distress; (2) prolonged progressive increase in dyspnea, anorexia, irritability, occasional vomiting, cardiac failure, and death; (3) repeated episodes of respiratory distress and cardiac failure which respond well to oxygen and digitalis and which may last months or even years.

The purpose of this report is to document extensive clinical studies made in a 6-year-old child with endocardial fibroelastosis whose clinical findings differed from the usual.

Presented before the Western Society for Clinical Research, Jan. 30, 1953, Carmel, Calif.

From the Department of Pediatrics, University of Minnesota, Minneapolis, and the Department of Pediatrics, University of California School of Medicine at Los Angeles.

1. (*a*) Pototschnig, G.: Über die kongenitale diffuse Endokardhyperplasia des linken Ventrikels, Ztschr. ang. Anat. **4**:234, 1918. (*b*) Gross, P.: Concept of Fetal Endocarditis: General Review with Report of Illustrative Case, Arch. Path. **31**:163, 1941. (*c*) Sano, M. E., and Anderson, N. A.: Elastic Tissue Hyperplasia of Endocardium, ibid. **33**:533, 1942. (*d*) Weinberg, T., and Himmelfarb, A. J.: Endocardial Fibroelastosis (So-Called Fetal Endocarditis); Report of 2 Cases Occurring in Siblings, Bull. Johns Hopkins Hosp. **72**:299, 1943. (*e*) Cosgrove, G. E., Jr., and Kaump, D. H.: Endocardial Sclerosis in Infants and Children, Am. J. Clin. Path. **16**:322, 1946. (*f*) Craig, J. M.: Congenital Endocardial Sclerosis, J. Tech. Methods **30**: 15, 1949. (*g*) Mahon, G. S.: Idiopathic Hypertrophy of the Heart with Endocardial Fibrosis: Report of 2 Cases, Am. Heart J. **12**:608, 1936. (*h*) Collier, F. C., and Rosahn, P. D.: Endocardial Fibroelastosis, Pediatrics **7**:175, 1951. (*i*) Edmonds, H. W., and Seelye, W. B.: Endocardial Sclerosis: Review of Changing Concepts with Report of 6 Cases, ibid. **7**:651, 1951. (*j*) Hill, W. T., and Reilly, W. A.: Endocardial Fibroelastosis, A. M. A. Am. J. Dis. Child. **82**:579, 1951.

2. Adams, F. H., and Katz, B.: Endocardial Fibroelastosis: Case Reports with Special Emphasis on the Clinical Findings, J. Pediat. **41**:141, 1952.

REPORT OF A CASE

J. B. was a white boy born on Feb. 22, 1946. Aside from a mild degree of difficulty in breathing and swallowing during the first six months of life, he was thought to be well until 3½ years of age. In the subsequent two and one-half years of his life he was hospitalized a total of 472 days.

The onset of his first illness was October, 1949, at 3½ years of age, at which time there developed signs of an upper respiratory infection associated with a slight cough, increasing fatigability, and vomiting. These symptoms persisted and increased. The patient also had three short syncopal attacks associated with coughing and questionable pain in his chest. When he was first hospitalized two months later, there was evidence of cardiac failure, facial and pedal edema, cardiomegaly, and hepatomegaly. At this time a to-an-fro murmur was heard in the fourth intercostal space to the left of the sternum and the quality of the heart tones was described as poor. As seen in Figure 1*A* and *B*, x-ray examination of the chest revealed a diffusely enlarged heart with a prominent left auricle and a convex pulmonary artery segment. At fluoroscopy there were poor pulsations. As seen in Figure 2, an electrocardiogram revealed a tendency to right axis deviation, notched P waves, isoelectric ST segments, and a P-R interval of 0.16 second with a rate of 120 per minute. It was thought by the clinicians at this time that the patient had an acute myocarditis, possibly of rheumatic origin, in spite of the absence of other rheumatic manifestations.

The treatment consisted of digitalis and bed rest. The patient gradually improved, and by one month later digitoxin therapy was stopped. X-rays at that time showed a 1.0 cm. decrease in the transverse diameter of the heart, the electrocardiogram was normal except for the notched P waves and, clinically, the patient appeared well. Apical systolic and diastolic murmurs were still audible over the precordium, however.

In the course of the next year the boy had six more hospitalizations because of repeated episodes of cardiac failure, prompted usually by a febrile episode or a respiratory infection. On each of these occasions he responded to bed rest and digitalis. X-rays of the heart and electrocardiograms remained essentially unchanged, as did the clinical findings. The diagnoses variously entertained were as follows: (1) rheumatic myocarditis with mitral stenosis and insufficiency; (2) interatrial septal defect; (3) Lutembacher's syndrome.

The patient was first seen at the university hospitals at 5 years of age, again in heart failure. The findings were much the same as on previous occasions, except for anasarca. Once again the patient responded to digitalis, bed rest, and mercurial diuretics and within the course of 10 days his weight fell from 55 to 46 lb. (24.9 to 20.9 kg.).

Three weeks after admission to the university hospital a cardiac catheterization was performed in order to learn more about the nature of the lesion present. Considerable time was spent on exploration of the interatrial septum with the catheter tip, and no evidence of a defect was found. From the collected studies, as seen in Table 1, the postcatheterization conclusion was that the patient had a pulmonary hypertension but structurally a normal right heart and that mitral stenosis and insufficiency existed, probably on the basis of a nonspecific myocarditis.

Less than a week following his discharge from the hospital, the patient returned, again decompensated. The clinical findings remained essentially the same. The left border of the heart was percussed 10.5 cm. to the left of the midsternal line. There was a palpable systolic thrill in the mitral area and a Grade IV systolic murmur was best heard in the third and fourth left interspaces. There was a Grade II diastolic murmur, plus a third heart sound in the fourth intercostal space at the nipple line. The x-rays of the heart and the electrocardiogram were essentially unchanged.

The child again responded to bed rest, digitalis, and meralluride (Mercuhydrin); however, his edema did not completely disappear. His serum proteins were then found to be surprisingly abnormal, a total of 3.5 gm. per 100 cc. with 1.4 gm. per 100 cc. albumin and 2.2 gm. per 100 cc. globulin.[3] Venous pressure measured in the antecubital vein was 10.2 cm. of water. Findings on repeated urinalyses were negative for albumin.

3. Total protein was determined by the Biuret method. The globulin was precipitated out, 26% sodium sulfate being used.

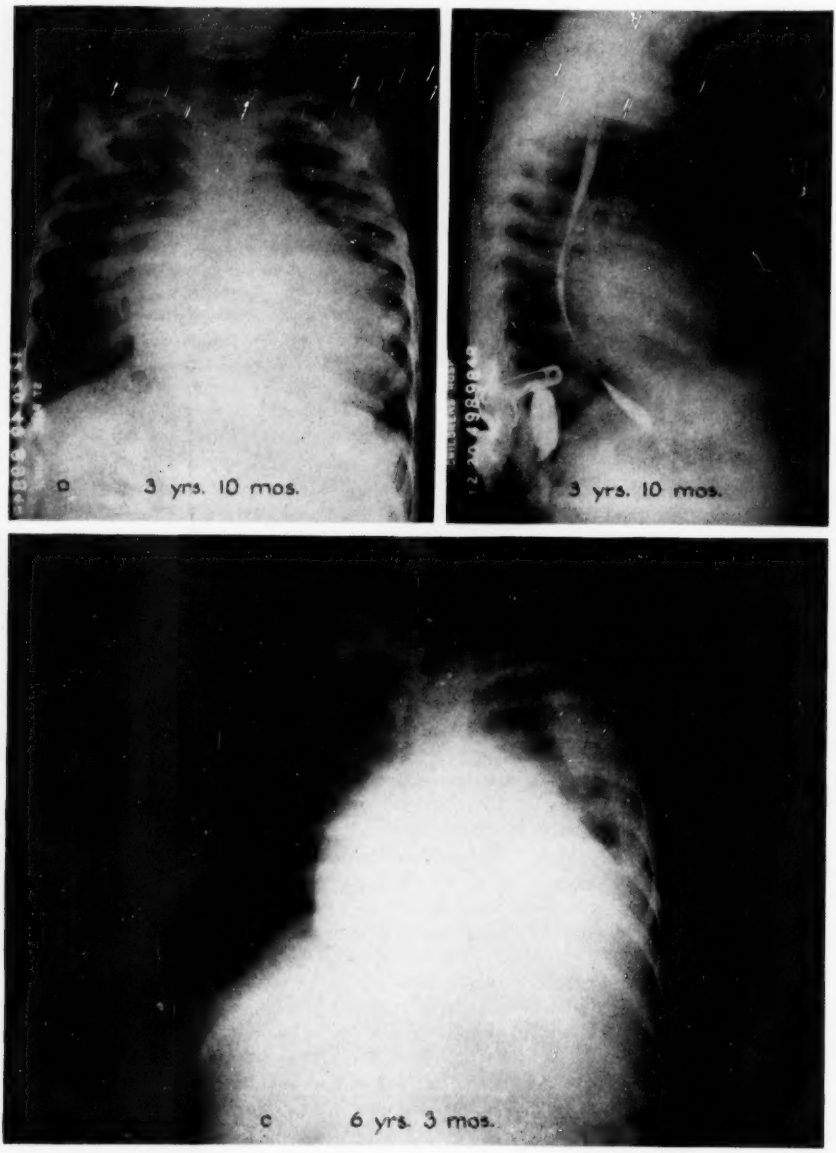


Fig. 1.—*A*, initial roentgenogram taken in the posteroanterior view at the age of 3 years 10 months. Note the diffuse cardiac enlargement, the convex pulmonary artery segment, and the increased pulmonary vascular markings. *B*, roentgenogram taken in the lateral view at same time as *A*. Note displacement of barium-filled esophagus indicating an enlarged left atrium. *C*, final roentgenogram taken in the posteroanterior view at age 6 years 3 months. Note the further diffuse enlargement of the heart with an increase in the convexity of the pulmonary artery segment. Marked pleural effusion is also present on the left side with the trachea and mediastinum shifted to the right.

Attempts were made to gain further insight into the origin of the hypoproteinemia. Other liver function tests revealed a negative cephalin-cholesterol test, a normal prothrombin time, sulfobromophthalein sodium retention of 6% in 45 minutes, and thymol turbidity of three units. However, tests for pyruvates [4] revealed a borderline elevation in both blood and urine. These were thought to be abnormal because the child had been receiving multiple vitamins daily. Renal function studies failed to disclose any gross defect in function. As was stated, findings on repeated urinalyses were negative for albumin. The patient had the ability to concentrate his urine to 1.019, the blood urea nitrogen was 18 mg. per 100 cc., the phenolsulfonphthalein dye test revealed 40% excretion in 60 minutes, and an intravenous pyelogram was normal.

A review of the dietary history showed that the patient had had an adequate protein intake in infancy and during the first four years of life. However, the protein intake had been poor during the preceding six to nine months. Attempts were therefore made to increase his pro-

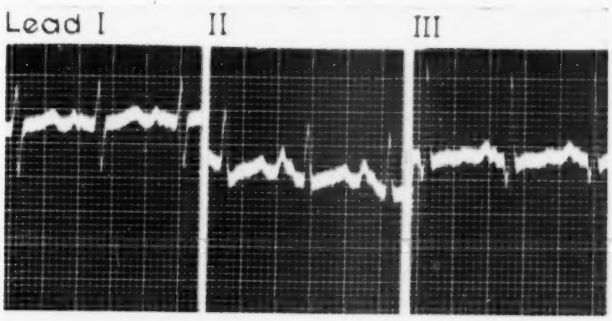


Fig. 2.—Initial electrocardiogram taken at age 3 years 10 months. Note the tendency to right axis deviation, the notched P waves, the isoelectric ST segments, and the P-R interval of 0.16 second with a rate of 120 per minute.

TABLE 1.—*Heart Catheterization Studies in Patient J. B.*

	% Oxygen Saturation	Mm. of Hg Pressure
Right pulmonary artery	63%	46/25
Main pulmonary artery	64%	46/32
Right ventricle	68%	45/0
Right atrium	69%	.....
Innominate vein	67%	.....
Femoral artery	97%	.....

tein intake. The child was placed on a diet from which he consumed between 70 to 100 gm. of protein a day. After approximately 10 days on this diet, the total serum protein was essentially unchanged (3.7 gm. per 100 cc. with 2.4 gm. per 100 cc. of albumin and 1.3 gm. per 100 cc. of globulin).

For the ensuing three months, a daily record was kept of the protein and caloric ingestion. This varied considerably from day to day depending upon the child's appetite. His average daily intake over this period was 2 gm. of protein per kilogram of body weight. Throughout this time, the patient was on bed activity only and, in spite of this intake, his serum proteins remained unchanged, as shown in Figure 3.

4. Platt, B. S., and Lu, G. D.: Studies on Metabolism of Pyruvic Acid in Normal and Vitamin B_1-Deficient States: Accumulation of Pyruvic Acid and Other Carbonyl Compounds in Beri-Beri and Effect of Vitamin B_1, Biochem. J. **33**:1525, 1939. Friedemann, T. E., and Haugen, G. E.: Pyruvic Acid: Determination of Keto Acids in Blood and Urine, J. Biol. Chem. **147**:415, 1943.

Other methods of correcting the existing hypoproteinemia were tried. Nine hundred cubic centimeters of plasma were given intravenously over a five-day period, but this did not change the serum protein level significantly. The patient was then given 30 gm. of salt-free human albumin intravenously over the course of one week. This, too, resulted in no change in the concentration of his serum proteins, but was followed by an increase in his edema; this was

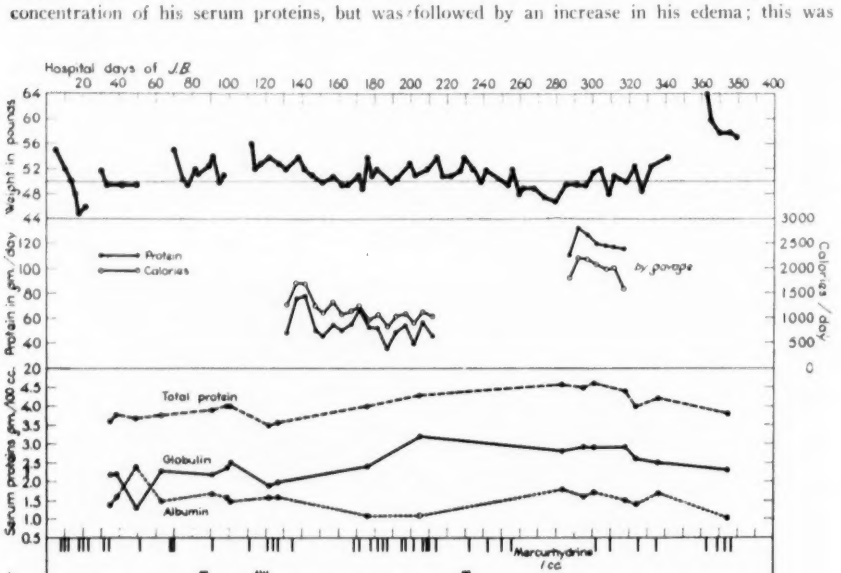


Fig. 3.—Graph showing the relationship between the body weight, total and fractional serum proteins, the total caloric, and the total protein intake. Note the failure of large amounts of protein provided either intravenously or by mouth to affect the serum protein level.

TABLE 2.—*Nitrogen Balance Studies in Patient J. B.*

Day	Intake, Gm.	Urine, Gm.	Feces, Gm.	Balance, Gm.
1	8.74	5.48	3.13	+ 0.14
2	8.74	1.51	3.13	+ 2.11
3	8.74	4.03	3.13	+ 1.59
4	8.74	3.64	3.13	+ 1.97
5	8.74	1.69	3.13	+ 3.92
6	8.74	7.25	1.76	— 0.26
7	8.74	1.55	1.76	+ 5.44
8	5.99	4.57	1.76	— 0.33
9	8.74	6.56	1.76	+ 0.42

then thought to be due to an overloading effect. A trial on testosterone propionate, 25 mg. daily, for its anabolic effect and intensive thiamine chloride therapy failed to have any effect on his ability to convert dietary to serum proteins, as seen in Figure 3.

On the assumption that this boy might have had such a prolonged protein starvation that all previous attempts to replenish the stores had been inadequate, he was then given gavage feedings of high-caloric high-protein content. Over a month's time, his daily intake was carefully recorded. The mean values were approximately 2,000 calories and 120 gm. of protein per day.

For nine days during this period, nitrogen balance studies were made. As seen in Table 2, the patient was in positive nitrogen balance for at least this short interval. The last four days of the study, the patient was receiving 25 mg. of testosterone propionate daily.

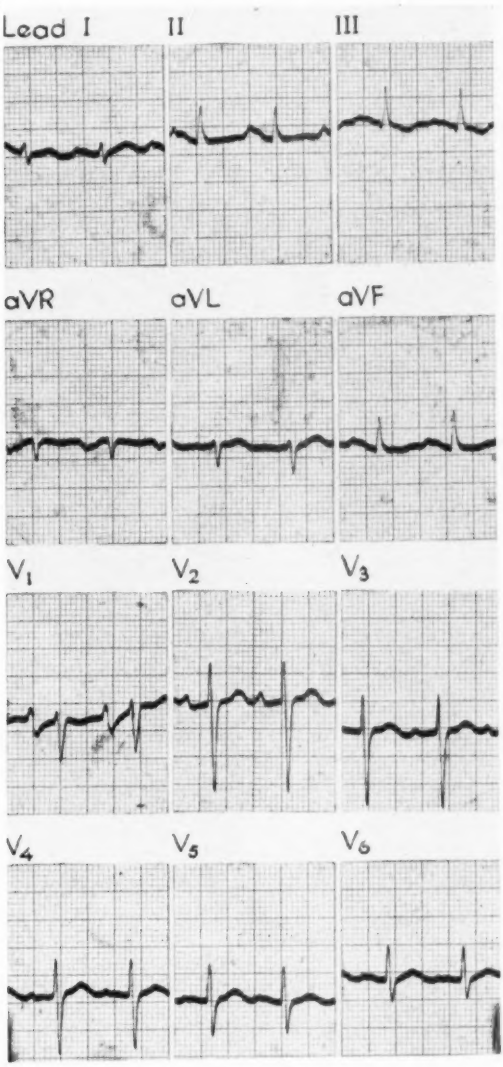


Fig. 4.—Final electrocardiogram taken at age 6 years 3 months. Note the tendency toward right axis deviation, the low voltage, the notched P waves, the prolonged P-R interval (0.20), and the T-wave changes.

In spite of this nutritional therapy, the serum protein values remained unchanged, as did his weight. Throughout this period, the serum cholinesterase was followed, and the values ran consistently low; the patient consistently showed values of 0.33 change in pH per hour, the normal being between 0.7 and 1.2.

Although these various therapeutic trials actually failed to cause any real change in his hypoproteinemia or his edema, he seemed better clinically. He was discharged from the hospital and was followed in the outpatient clinic on a high-protein diet.

One month later acute cardiac decompensation forced rehospitalization. The physical findings were similar to those noted previously and he was in acute cardiorespiratory distress. As seen in Figure 1*C*, x-rays of the heart revealed a pleural effusion on the left with mediastinal shift to the right. The electrocardiogram showed a somewhat diminished voltage from that previously noted; there still remained a tendency toward right axis deviation, as seen in Figure 4. At first the child seemed to respond to diuretics, digitalis, and rest. He lost approximately 5 lb. (2.3 kg.) and seemed improved for the first week. Gradually he became more listless, and

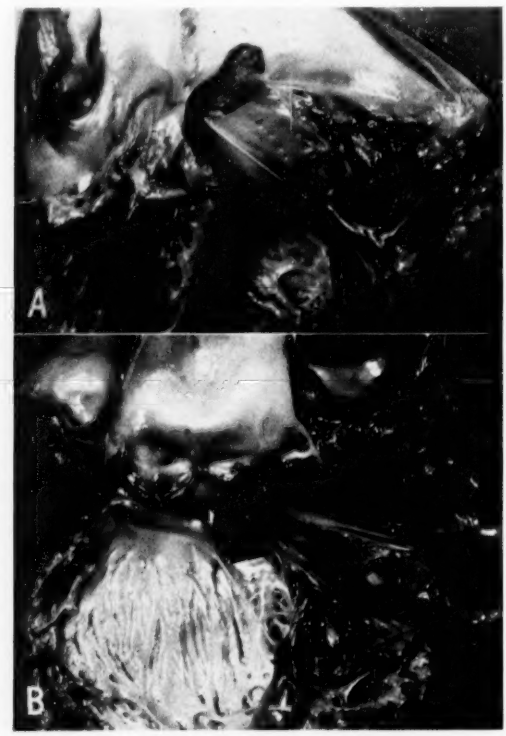


Fig. 5.—Photographs of the heart: *A*, showing the thickened mitral valve leaflets that produced the mitral insufficiency; *B*, showing the thick gray-colored endocardium of the left ventricle.

his weight again began to increase slowly. Respiratory distress increased and it became evident that the patient was failing. He died on the 19th hospital day at 6 years 3 months of age.

Pathological Findings.—The postmortem findings of significance were limited to the heart and liver. The patient had moderate amounts of pleural and ascitic fluid, but there was only a minimal amount of fluid in the pericardial sac.

The heart appeared to be generally large and weighed 300 gm. There was no evidence of pericarditis. The great vessels were normal and the ductus arteriosus was closed. Internal examination revealed the foramen ovale to be closed. The tricuspid valve showed but slight rolling and thickening of the edges but the mitral valve showed marked rolling of the edges with calcification and thickening of the valve as seen in Figure 5*A*. The pulmonary and aortic valves both appeared to be normal. The interventricular septum was intact.

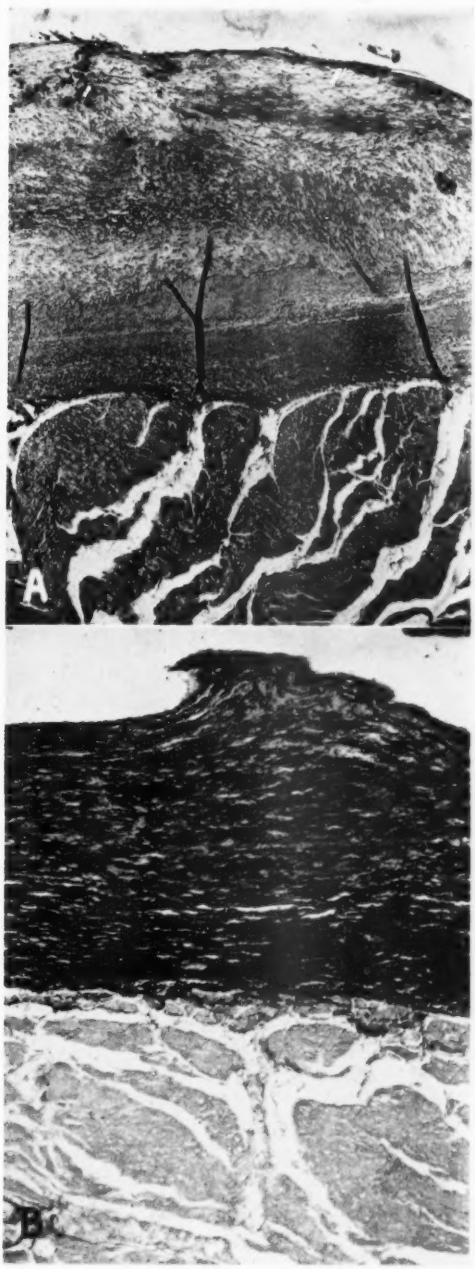


Fig. 6.—Photomicrographs of the endocardium and the myocardium from the left ventricle. *A*, hematoxylin and eosin stain. *B*, elastic tissue stain. Magnification × 90. Note the enormous increase in the thickness of the endocardium which is composed primarily of elastic tissue fibers.

The internal surface of the left ventricle had a shiny white appearance which penetrated to some degree into the myocardium, as seen in Figure 5*B*. This same process was present, but to a lesser degree, in the left atrium. The endocardial surface on the right side appeared normal. The thickness of the left ventricle was 1 cm., and that of the right ventricle was 0.7 cm. The coronary arteries arose from the aorta in the normal manner.

The weight of the liver was 630 gm., and cut section of the right lobe showed a yellowish discoloration. The left lobe appeared normal.

The other organs appeared grossly normal except for the presence of a Meckel's diverticulum and an accessory spleen.

On microscopic study, the heart muscles showed subendocardial thickening which, on Weigert stain, proved to be elastic fibers typical of subendocardial fibroelastosis, as seen in Figures 6*A* and *B*. The mitral valves, as seen in Figure 7, showed enlargement and thickening of the edges with subendocardial fibrosis. No Aschoff bodies were seen, but there were aggregates of

Fig. 7.—Photomicrograph of a section from the mitral valve stained with hematoxylin and eosin. Magnified 15 ×. Note the marked increase in the thickness of the endocardium.

inflammatory cells around a few of the vessels within the myocardium. The liver showed pericentral degeneration, dilatation of the sinusoids, and separation of the liver cords, as seen in Figure 8.

COMMENT

Hyperplasia of the endocardium has been a known pathologic entity for the past three decades. Pototschnig [1a] in 1918 described the condition as have many authors since.[5] Only recently have papers appeared suggesting the clinical course of such patients.[6] In another communication we have reviewed the clinical pattern

5. Footnotes 1 *b*, *c*, *d*, *e*, *f*, *g*, *h*, *i*, *j*, and 2.

6. Adams and Katz.[2] Lewis, K. C.: Cardiac Enlargement of Unknown Etiology in Infancy and Childhood, J. Pediat. **39**:698, 1951.

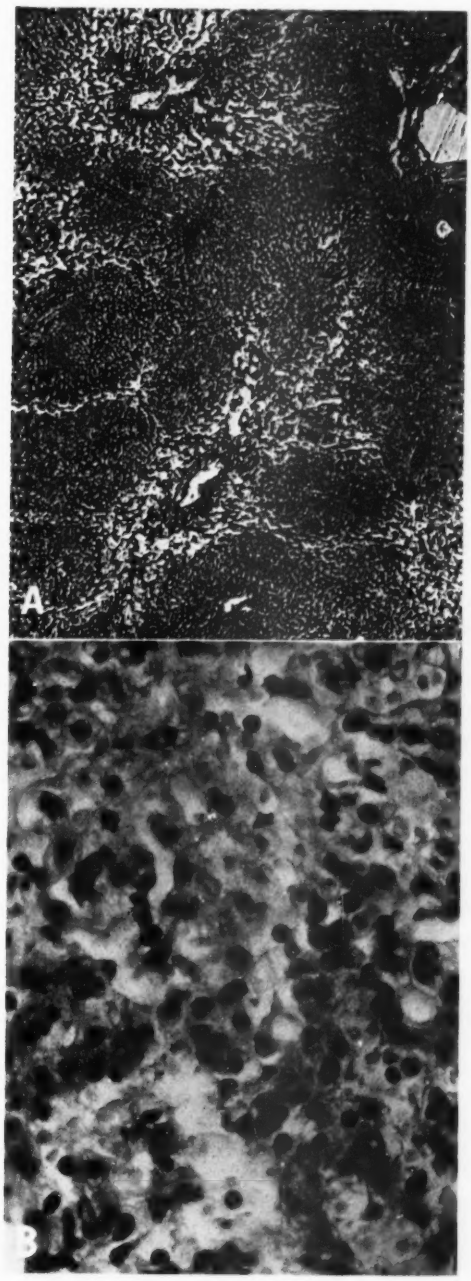


Fig. 8.—Photomicrographs of the liver: *A*, showing the relatively normal structure at magnification × 15. *B*, showing some dilatation of the sinusoids and separation of the liver cords at magnification × 430.

of 21 patients and have outlined the common signs and symptoms, and the physical and laboratory findings.[2] The present patient's condition was not properly diagnosed ante mortem; however, the diagnosis of endocardial fibroelastosis was considered as a possibility in the differential diagnosis at one time because of the absence of any of the usual findings of congenital heart disease, as shown by cardiac catheterization, and the clinical evidence of mitral heart disease.

In restrospect, other features of this patient's condition which were compatible with the diagnosis of endocardial fibroelastosis were the repeated episodes of myocardial failure, usually initiated by an intercurrent infection. The favorable response to digitalis and rest was repeatedly shown. The age of onset in this patient was somewhat older than has been noted heretofore, and it would appear that this patient is the oldest in any case reported with autopsy findings.

There are several other features considered to be unusual about this case. One was the diffuse enlargement of the heart rather than the usually observed left-sided changes. This might have been anticipated as a result of the mitral lesion producing cor pulmonale with resultant right, as well as left, ventricular enlargement. The electrocardiograms were never thought to be typical of those frequently seen in endocardial fibroelastosis although the digitalis effect might well have masked the anoxic changes expected (ST depressions and T wave inversion). At no time was a left axis deviation noted.

Aside from the condition of the heart in this case, the implication of the effect of repeated episodes of decompensation upon liver functions is of equal interest. In our experience with subendocardial fibroelastosis a hypoproteinemia has not been previously noted. That severe chronic passive congestion of the liver can result in impairment of the serum-protein-fabricating function has been shown in cases of chronic constrictive pericarditis by McQuarrie[7] and Stadler and Stinger.[8] Sherlock,[9] in reviewing liver function studies in adults with varied forms of heart disease which prompted repeated episodes of decompensation, found the serum proteins to be generally unaffected by cardiac failure. However, in the cases that did show lower serum albumin levels, but most common lesions were mitral stenosis and cor pulmonale, both of which this patient had. Apparently in our patient the effect of passive congestion upon the liver was relatively specific for its ability to handle pyruvates. In the metabolism of pyruvates it has been shown that thiamine is converted to diphosphothiamine and this acts as a coenzyme in the final catabolism of pyruvic acid.[10] It is also accepted that the liver is the site for this conversion of thiamine. In our patient adequate thiamine was administered, yet the blood pyruvates remained elevated. Thus it seems reasonable to assume that the liver function for this conversion was abnormal.

7. McQuarrie, I.: Impaired Ability to Fabricate Serum Proteins the Chief Cause of Edema in Chronic Constrictive Pericarditis, Journal-Lancet **62**:199,, 1942.

8. Stadler, H., and Stinger, D. I.: Case of Pick's Syndrome as Basis for Study of Hypoproteinemia, J. Pediat. **18**:84, 1941.

9. Sherlock, S.: The Liver in Heart Failure: Relation of Anatomical, Functional and Circulatory Changes, Brit. Heart J. **13**:273, 1951.

10. Westerfeld, W. W.; Stotz, E., and Berg, R. L.: Role of Pyruvate in Metabolism of Ethyl Alcohol, J. Biochem. **144**:657, 1942. Stotz, E.: Pyruvates, Advances in Enzymology **5**:129, 1945.

Measurement of serum cholinesterase,[11] which actually is a pseudocholinesterase as opposed to that of nervous tissue, has been shown to be a sensitive index of hepatocellular function. The actual function of this substance is as yet uncertain. It may be decreased with varied types of liver disease as well as malnutrition.[12] It has been pointed out by Kunkel,[13] Vorhaus,[14] and others, however, that there is a parallelism between the serum cholinesterase level and the synthesis of serum albumin. Whether it is low as a function of albumin or as a result of the same process which produces albumin has not been determined. The interpretation of the values in our patient does substantiate the findings of low values associated with hypoproteinemia. It is considered in this instance to be a possible indication of hepatic dysfunction, perhaps, of the ability of the liver in its function of protein synthesis.

The etiology of subendocardial fibroelastosis still remains a matter of conjecture. Hill and Reilly [1] have suggested its relation to the collagen diseases. We have been unwilling to accept this hypothesis.[2]

An interesting possibility of the relationship of endocardial fibroelastosis to nutritional deficiencies is suggested by our patient and also the writings of Davies [15] and others on the African disease kwashiorkor. Kwashiorkor is a condition which affects children between the ages of 6 months and 5 years and is characterized by anasarca, hypoproteinemia, and findings in the heart of degeneration of myocardial fibers, especially in the subendocardial region. Subsequently, fibrous tissue forms as white plaques involving all the cardiac chambers, especially the apices of the ventricles and particularly that of the left. There are obvious differences between kwashiorkor and endocardial fibroelastosis but, because superficially our patient's disease resembled kwashiorkor, it must be added to the differential diagnosis.

SUMMARY

The case history and the physical, laboratory, and postmortem findings in a patient having endocardial fibroelastosis have been presented. This patient is the oldest in reported cases to be examined post mortem. The unusual features were the somewhat atypical physical findings, particularly the persistent edema. After extensive study, it was concluded that the edema was, in part, due to low plasma proteins, secondary to impaired ability of the liver to fabricate such proteins.

Dr. Irvine McQuarrie, Professor of Pediatrics, aided in the studies performed and in the preparation of the manuscript; Dr. Mildred Ziegler performed the balance studies, and Dr. E. Frame performed the pyruvate and cholinesterase studies.

11. Michel, H. O.: Electrometric Method for the Determination of Red Blood Cell and Plasma Cholinesterase Activity, J. Lab. & Clin. Med. **34**:1564, 1949.

12. McCance, R. A.: Serum Cholinesterases in Undernutrition, Proc. Royal Soc. Med. **43**: 272, 1950.

13. Kunkel, H. G., and Ward, S. M.: Plasma Esterase Activity in Patients with Liver Disease and the Nephrotic Syndrome, J. Exper. Med. **86**:325, 1947.

14. Vorhaus, L. J., II; Scudamore, H. H., and Kark, R. M.: Measurement of Serum Cholinesterase Activity in the Study of Diseases of the Liver and Biliary System, Gastroenterology **15**:304, 1950.

15. Davies, J. N. P.: Nutrition and Nutritional Diseases, Annual Review of Medicine, Stanford, Calif. Annual Review Inc., 1952, Vol. 3, p. 99.

CONGENITAL MYASTHENIA GRAVIS

RHETT P. WALKER, M.D.
BIRMINGHAM, ALA.

MYASTHENIA gravis is rare, but does occur in the newborn. In the child of a myasthenic mother one occasionally sees the typical clinical picture. If the child survives the neonatal period, the disease disappears spontaneously in a few days or weeks.

The other type of myasthenia gravis occurring in the newborn is rarer and occurs in children born of healthy mothers. Their disease resembles the adult type and tends to be permanent. It is the purpose of this communication to report such a case.

REPORT OF CASE

A 2-month-old white girl was admitted to the Children's Hospital on Nov. 27, 1951, for study of respiratory difficulty and inability to nurse.

There was no family history of myasthenia gravis or other muscular or nervous diseases. Gestation was remarkable in that the mother was intimately exposed to an acute case poliomyelitis early in her pregnancy. Delivery was preceded by a week of frequent vomiting. The baby was full term and was born at home without difficulty. The birth weight was 8 lb. 2 oz. (3,690 gm.).

It was noticed from birth that the child was feeble and limp. Her cry was weak. For the first four days of life she nursed the breast very poorly. She improved slightly, but about the seventh day her parents noticed milk running from her nose. She continued to nurse with difficulty until she was about one month old. At this time she was seen by a physician who had her taken from the breast and given a formula. She was able to take only about 1 oz. (30 ml.) of this at a time. Several weeks later she began having trouble breathing, apparently because she could not expel the secretions in her pharynx. On several occasions she became cyanotic on attempted feeding and had to be maintained on tube feedings and frequent suctioning.

Admission examination revealed a limp, inactive, somewhat undernourished, fairly well-developed, well-hydrated infant. She was having considerable respiratory difficulty. Positive physical findings included the following: The eyelids were slightly ptotic. There was a thin watery nasal discharge. The lips had a slight bluish tinge. The pharynx contained a large amount of watery secretions. The cry was feeble. Rhonchi were heard throughout the lung fields. Neurological examination showed hypoactive deep reflexes. The blood cell count and the findings on urinalysis were normal, and the results of the Kahn test were negative.

Findings on fluoroscopy of the chest were normal. Examination of the pharynx, the hypopharynx, and the larynx revealed no anatomic deformities. It was observed that the gag reflex was hypoactive and that movements of the pharynx and the soft palate were slow. Iodized oil (Lipiodol) injected into the esophagus progressed normally to the stomach. No fistula or atresia was demonstrated. Iodized oil injected into the trachea showed nothing abnormal. The impression at the time was of pharyngeal weakness or paralysis, possibly from a bulbar lesion. Poliomyelitis, nuclear aplasia, amyotonia congenita, birth injury to the brain stem, and myasthenia gravis were considered.

A therapeutic trial with neostigmine (Prostigmine) was begun. Within an hour her respiration and expulsion of the secretions had considerably improved. She took 3 oz. (89 ml.) of formula without difficulty. This was the first time in three weeks she had taken milk from a bottle. She became more alert and active, and her partial ptosis disappeared. On several occa-

From the Department of Medicine, Medical College of Alabama, Birmingham, Alabama.

sions attempts were made to decrease the dose or increase the interval, but this was met each time by a return of symptoms.

After much adjustment of the dosage schedule, the child was discharged four weeks after admission fairly well regulated on a regimen of 7.5 mg. of neostigmine bromide every eight hours, administered orally. Four days later she was readmitted because of a return of symptoms. The dosage was modified to 5 mg. every four hours. She was discharged two weeks later, improved.

When last heard from, at 8 months of age, it was reported that she was still taking neostigmine and getting along fairly well.

COMMENT

Survey of the literature reveals 17 reported instances of congenital myasthenia gravis. Thirteen cases of the transient type occurring in the offspring of myasthenic mothers have been reported. One might speculate that there is circulating in the mother's blood some material which inhibits the formation of acetylcholine or

Previously Reported Cases of Myasthenia Gravis

Authors	Outcome
Nonmyasthenic mothers	
Mackay [1a]	Child 9 yr. old; retarded physically; still on neostigmine (Prostigmine)
Bowman [1b]	Child 3½ yr. old; still on neostigmine
Levin [1c]	Died at 10 yr.; pneumonia
Levin [1c]	Recovered from disease at 9 yr.
Myasthenic mothers	
Nilsby [1d]	Neostigmine discontinued at 1 mo.
Strickroot [1e]	Died on 6th day
Geddes [1f]	Neostigmine discontinued at 36 days
Wilson *	No neostigmine; died on 4th day
Wilson *	No neostigmine; careful nursing; improved 2nd wk.
Stone *	Neostigmine discontinued 13th day
Ford *	Neostigmine discontinued at 1 wk.
LaBranche [1g]	Still on neostigmine at 4 mo., no attempt to discontinue after 1 mo.
Viets [1h]	3 patients recovered during neonatal period
Holt †	Recovered during neonatal period
McKeever [1i]	Child recovered in 3 wk.

* Quoted by Geddes.[1f]
† Quoted by Viets.[1h]

accelerates its destruction. This substance is presumably destroyed or excreted by the infant during the neonatal period.

Four reported cases were in children of nonmyasthenic mothers. The patient reported here belongs to this group. Their disease tends to be permanent. The previously reported cases [1] are summarized in the accompanying Table.

1. (*a*) Mackay, R. I.: Congenital Myasthenia Gravis, Arch. Dis. Childhood **26**:289-293 (Aug.) 1951. (*b*) Bowman, J. R.: Myasthenia Gravis in Young Children: Report of Three Cases—One Congenital, Pediatrics **1**:472-477 (April) 1948. (*c*) Levin, P. M.: Congenital Myasthenia in Siblings, Arch. Neurol. & Psychiat. **62**:745-758 (Dec.) 1949. (*d*) Nilsby, J.: Myasthenia Gravis of Newborn Child, Acta pædiat. **37**:489-492, 1949. (*e*) Strickroot, F. L.; Schaffer, R. L., and Bergo, H. L.: Myasthenia Gravis Occurring in Infant Born of Myasthenic Mother, J. A. M. A. **120**:1207-1209 (Dec. 12) 1942. (*f*) Geddes, A. K., and Kidd, H. M.: Myasthenia Gravis of Newborn, Canad. M. A. J. **64**:152-156 (Feb.) 1951. (*g*) LaBranche, H. G., and Jefferson, R. N.: Congenital Myasthenia Gravis, Pediatrics **4**:16-20 (July) 1949. (*h*) Viets, H. R. and Brown, M. R.: Medical Progress: Diseases of Muscles, New England J. Med. **245**:647-653 (Oct. 25) 1951. (*i*) McKeever, G. E.: Myasthenia Gravis in a Mother and Her Newborn Son, J. A. M. A. **147**:320-322 (Sept. 22) 1951.

SUMMARY AND CONCLUSIONS

Myasthenia gravis reaches its peak incidence in the third and fourth decades and is rare in the newborn. In the child of a myasthenic mother one may see the typical picture. If the child survives the neonatal period, the disease disappears spontaneously in a few days or weeks. Thirteen such cases have been reported.

The other type is rarer and occurs in children born of healthy mothers. Their disease tends to be permanent. Four such cases have been reported. A patient with this type of congenital myasthenia gravis is here reported.

Progress in Pediatrics

DIARRHEA OF ALLERGIC ORIGIN

A Review

PHILLIP E. ROTHMAN, M.D.
BEVERLY HILLS, CALIF.

Gastrointestinal allergy is a diagnosis frequently entertained, occasionally evaluated and rarely established. It offers, to its enthusiastic supporters, a reasonable explanation for many obscure abdominal complaints. To the skeptical, it frequently appears as a specious and unwarranted diagnosis.

THESE introductory sentences which appear in the review by Ingelfinger, Lowell, and Franklin [1] reflect the present status of this form of allergy. Evidence to support this diagnosis has been grouped into three categories: experimental studies, clinical observations, and laboratory tests. A brief summary of their conclusions is helpful in the interpretation of the general aspects of intestinal allergic disorders.

Experimental studies should theoretically be designed to fulfil the following requirements: "Symptoms should be caused by contact with a specific substance that is innocuous to the bulk of the population; an immune mechanism should be evident in their pathogenesis; lesions and functional changes in the gut should be demonstrable." In this respect the work of Walzer and his co-workers [2] is most informative. They injected serum obtained from a patient highly sensitive to peanuts into the skin of the arm, into the rectal mucosa, and into the intestinal mucosa in patients with ileostomy and colostomy. An allergic reaction was induced at these sensitized areas by the oral administration of the antigen, by its introduction into any part of the bowel, or by its direct application locally to the sensitized mucous membrane sites. The mucous membrane, despite its direct contact with the antigen, did not react maximally until the antigen became generally disseminated by way of the circulation. The allergic reaction in the mucous membrane was characterized by edema, hyperemia, and excessive mucus secretion.

Clinical observations depend largely on histories of an apparent relationship between the ingestion of a suspected food and the subsequent onset of one or more symptoms such as nausea, vomiting, distention, colic, and diarrhea. The following case described by Ingelfinger illustrates the difficulties in diagnosis:

A twenty-year-old girl stated that she could not eat fish because it caused vomiting and asthma; even getting near a fish market caused these symptoms. Skin reactions to fish were strongly positive. However, a freshly prepared fish extract, also causing a marked skin reaction of the immediate type, was introduced into the stomach by stomach tube in a manner to

1. Ingelfinger, F. J.; Lowell, F. C., and Franklin, W.: Medical Progress: Gastrointestinal Allergy, New England J. Med. **241**:303, 1949.

2. Walzer, M.: Allergy of the Abdominal Organs, J. Lab. & Clin. Med. **26**:1867, 1941. Gray, I.; Harten, M., and Walzer, M.: Studies in Mucous Membrane Hypersensitiveness: IV. Allergic Reaction in Passively Sensitized Mucous Membranes of Ileum and Colon in Humans, Ann. Int. Med. **13**:2050, 1940.

prevent the patient from knowing that fish was being introduced. No symptoms occurred, and there was no change in the stomach or intestine by fluoroscopy. Furthermore, no delayed symptoms occurred.

The belief that symptoms always follow the ingestion of an offending food within a period of 1 to 12 hours is almost certainly an error as judged by careful clinical observations. It seems likely that sensitivity may be variable, quantitative, cumulative, and related to intercurrent infections of the intestinal tract. A personal or family history of hay fever, asthma, eczema, or hives in a patient with gastrointestinal symptoms merely suggests an allergic tendency, but in no way establishes the diagnosis. Similarly, the absence of other allergic manifestations should not be construed as evidence unfavorable to the diagnosis.

Laboratory tests are unfortunately of little aid in diagnosis. Roentgenologic studies with the use of a barium-in-water meal followed in a few days by a similar examination plus the suspected food, administered either with the barium or a few hours later, will frequently show, on the second test, delayed gastric emptying time and changes in intestinal motility. Similar findings occur in asymptomatic individuals, and the test would be of significance only if accompanied by more extensive control studies. A few direct observations of the gastric mucosa have revealed transient urticarial edema 30 to 60 minutes after the ingestion of a suspected food. The conclusions of Ingelfinger and his co-workers in respect to skin tests are as follows:

> Most workers have been discouraged with attempts to apply skin tests to the diagnosis of gastrointestinal allergy. Positive skin reactions, though generally regarded as indicating allergic sensitivity of the skin to the substance injected, do not necessarily indicate similar sensitivity of the gastrointestinal tract, nor are negative reactions considered adequate evidence on which to exclude it. These views are based on the absence of correlation between the reaction observed in the skin and the occurrence of gastrointestinal symptoms on exposure of the patient to the substance from which the extract was made.

Variations in the number of leucocytes, eosinophiles, or thrombocytes following the ingestion of foods have not proved reliable tests. The presence of eosinophiles in fecal mucus has been found in necrotic neoplasms of the intestine, ulcerative colitis, and amebic dysentery, as well as in intestinal allergic disorders.

It is the purpose of this review to discuss some clinical phases of a single manifestation of gastrointestinal allergy, namely diarrhea, and to limit the discussion chiefly to infants under 2 years of age. It is generally believed that the pathogenesis of food allergy in infancy arises rarely as the result of sensitization in utero and more often from the passage of orally administered proteins through the intact intestinal wall. This mechanism of sensitization described originally by Schloss and Worthen [3] has been corroborated by many investigators.[4] Thus Walzer [5] fed egg-white antigen mixed with formula to newborn infants who had been passively locally sensitized and noted a positive reaction before they had finished their bottles. He concluded that in respect to unaltered proteins the gastrointestinal tract of the

3. Schloss, O. M., and Worthen, T. W.: The Permeability of the Gastro-Enteric Tract of Infants to Undigested Protein, Am. J. Dis. Child. **11**:342, 1916.

4. Lippard, V. W.: Immunologic Response to Ingestion of Foods by Normal and by Eczematous Infants, Am. J. Dis. Child. **57**:524, 1939.

5. Walzer, M., in discussion on Bell, S. D.: Transfer of Skin Sensitizing Antibodies, J. Allergy **2**:399, 1931.

newborn infant is almost like a sieve. Evidence that a corresponding condition of the gastrointestinal tract may follow infectious colitis or enteritis in the adult is suggested by the observations of Rappaport [6] in cases of postdysenteric diarrhea due to milk allergy. Similarly it is not unusual to observe widespread urticaria in children when a regular diet is resumed following an attack of enteritis. From the information available cases with diarrhea as a single or principal manifestation of food allergy in infancy may be divided into two clinical groups: (1) severe diarrhea during the neonatal period with rapid loss of fluid and electrolytes and impending death; (2) chronic diarrhea during the second year of life simulating cases of celiac disease. Mild cases of diarrhea occur in both groups and with greater frequency than the severe cases. Only rarely can help be obtained from laboratory tests, and in general they represent a waste of time and money. Most important are careful and repeated stool examinations and cultures to avoid confusion with intestinal disturbances of a specific infectious origin. Marked stool eosinophilia [7] is usually present during the period of active symptoms. Precise methods of scientific evaluation are not available for the establishment of a diagnosis of gastrointestinal allergy, and many errors will continue to be made. There is no way of estimating with any degree of accuracy the incidence of this disorder.

A typical case report of the first group is contained in the recent article by Darrow [8] on the treatment of infantile diarrhea.

The patient weighed 3,100 gm. at birth and after transfer to an orphan asylum weighed 2,900 gm. on the seventh day. He did not thrive and was admitted to the hospital on the 31st day weighing 2,720 gm. Two days prior to admission diarrhea leading to dehydration and acidosis (119 mM. of Cl and 15 mM. of CO_2 per liter) developed. He responded to parenteral fluid therapy but continued to have diarrhea when fed. On the eighth day of treatment and the fifth day after milk was started, he was again fasted for 24 hours because of dehydration. He again responded to milk feeding with such severe diarrhea that recovery seemed impossible. He presented the picture which Finkelstein called "decomposition." He was again given parenteral fluids, 1 cc. of lipo extract of the adrenal cortex twice daily, and changed to Nutramigen (a food containing amino acids, fat, and carbohydrate—Mead Johnson). Within 24 hours the response was so favorable that recovery seemed likely. At that time it was not clear whether the favorable response was due to adrenal cortical extract or omission of milk. On the 78th day of life he again became sick from diarrhea following one bottle of milk. On the 93rd day of life he again received one bottle of milk by mistake. This time he vomited within two hours and such severe diarrhea developed that the weight decreased from 3,480 gm. to 2,840 gm. within 18 hours. Although gain in weight was unusually slow, he was discharged to a foster home on the 132nd day of life. He continued to be fed Nutramigen for a long time and was gradually able to return to cow's milk.

6. Rappaport, E. M.: Postdysenteric Diarrhea Due to Milk Allergy, Rev. Gastroenterol. **15**:466, 1948.

7. (*a*) Rosenblum, A. H., and Rosenblum, P.: Gastrointestinal Allergy in Infancy, Pediatrics **9**:311, 1952. (*b*) A satisfactory technic for demonstrating stool eosinophilia is described in the article by Rosenblum and Rosenblum. Smears are made from the mucoid portion of a fresh stool. A specimen obtained by insertion of the finger is satisfactory. The smear is allowed to dry without heat. Undiluted May-Grunwald stain is applied for 30 seconds. It is then diluted with an equal quantity of distilled water and allowed to stand an additional 30 seconds before the final washing. If the smear is too light, it may be restained by the same technique.

8. Darrow, D. C.: Therapeutic Measures Promoting Recovery from the Physiologic Disturbances of Infantile Diarrhoea, Pediatrics **9**:519, 1952.

Similar cases have been observed by many pediatricians. The often-quoted cases described by Rubin [9] showed intestinal bleeding as a prominent feature. Diarrhea may also occur in the hyperacute type of food sensitivity described by Schloss,[10] Park,[11] Richet,[12] Blackfan,[13] Talbot,[14] and others.[15] In these cases the associated symptoms of urticaria, vomiting, and shock and the obvious relationship to the offending food simplify the diagnosis. When diarrhea is the only manifestation of food allergy, the diagnosis is more difficult. This is particularly true if the diarrhea is not severe, and a slight but unsatisfactory gain in weight tends to mask the underlying disturbance. Cow's-milk sensitivity may appear at any age, but predominantly during the early months. The incidence of food allergy during the neonatal period appears to be increasing as the popularity of breast milk diminishes.

Darrow's [8] case illustrates the unavoidable loss of time in establishing a diagnosis and the constant danger of a fatal outcome. The conditions simulating this clinical picture are infectious diarrhea (bacterial, viral, and parenteral), pancreatic fibrosis, and adrenocortical insufficiency. The diarrhea in pancreatic fibrosis is rarely severe, the stools have characteristic peculiarities, respiratory symptoms are often present, and trypsin is usually deficient. In adrenocortical insufficiency, vomiting nearly always occurs, hypochloremia is present, and response to treatment with salt and desoxycorticosterone is dramatic. It becomes apparent that the principal differential diagnosis is with viral or nonspecific diarrhea. If the child was originally breast-fed, considerable aid may come from a history of intestinal disturbances associated with the introduction of cow's milk. An acute onset of diarrhea in a child who is progressing satisfactorily on cow's milk is in all likelihood infectious in origin. Accordingly, cow's milk allergy may be suspected early, and one must carefully guard against overenthusiasm in diagnosis and a failure to recognize the normal variations in the intestinal manifestations of the newborn. If the diarrhea is severe, it is advantageous diagnostically to withhold feeding for two or three days while the child receives parenteral fluids. A rapid response to the elimination of cow's milk and an immediate exacerbation of symptoms following the onset of feedings should lead to a suspicion of milk allergy. That it can be no more than a suspicion is unfortunately true, for the same sequence of events can occur with infectious diarrhea. The experiment is of greater value if the feeding is protein milk or skimmed lactic acid milk, for these preparations often have a beneficial effect on an infectious diarrhea, but will quickly produce an exacerbation in children with severe milk allergy. Once the diagnosis is suspected a therapeutic trial is in order. In addition to breast milk and goat's

9. Rubin, M. I.: Allergic Intestinal Bleeding in the Newborn: Clinical Syndrome, Am. J. M. Sc. **200**:385, 1940.

10. Schloss, O. M.: Allergy in Infants and Children, Am. J. Dis. Child. **19**:433, 1920.

11. Park, E. A.: A Case of Hypersensitiveness to Cow's Milk, Am. J. Dis. Child. **19**:46, 1920.

12. Richet, C., Jr.: Food Anaphylaxis, J. Allergy **2**:76, 1931.

13. Blackfan, K. D.: A Consideration of Certain Aspects of Protein Hypersensitiveness in Children, Am. J. M. Sc. **160**:34, 1920.

14. Talbot, F. B.: The Relation of Food Idiosyncrasies to the Diseases of Childhood, Boston M. & S. J. **179**:285, 1918.

15. Laroche, G.; Richet Fils, C., and Saint-Girons, F.: Alimentary Anaphylaxis: Gastro-Intestinal Food Allergy, translated by M. P. Rowe and A. H. Rowe, Berkeley, California, University of California Press, 1930.

milk several hypoallergenic formulas are available: Mull-Soy and Soyalac (soybean milks) Nutramigen; and a modification of the meat formula described by McQuarrie.[16] The original formula of McQuarrie is as follows:

Strained beef (canned)	100.0 gm.
Salt mixture (Ca-gluconate 6.3 gm., K_2HPO_4 1.0 gm., and Mg-citrate 0.4 gm.)	7.7 gm.
Lard	16.5 gm.
Rice (thoroughly cooked gruel)	16.0 gm.
Sucrose	12.8 gm.
Water	347.0 gm.

Ideally, a formula for small infants with any type of diarrhea should be low in fat and in carbohydrate if one is concerned with the appearance and number of stools and not the degree of absorption of each ingredient. Neither of the first two preparations meet this requirement, and both have a tendency to increase the number of stools. Hence an adverse reaction to these formulas will often confuse the diagnosis and lead to the erroneous conclusion that the diarrhea is on an infectious basis. Thus Glaser and Johnstone[17] fed soy bean milk to 67 supposedly normal infants and found that in 13.5% one or more of the following symptoms developed: diarrhea, vomiting, colic, and atopic dermatitis. Fortunately, dramatic success may occur as in Darrow's case. Both preparations should be diluted to one-third or one-fourth the standard strength and use started in very small amounts. More reliable is the meat formula, use of which should be started without the addition of fat and with very little carbohydrate. Formulas designed to meet, on the initial trial, the infant's complete nutritional requirements represent the commonest therapeutic error.

The milder cases of diarrhea in this group consist of infants with a limited tolerance to cow's milk. Treatment is indicated if the gain in weight is unsatisfactory. Many of these infants are in good health, have tremendous appetites, and do not require treatment. They are, unfortunately, often subjected to numerous experiments with a wide variety of proprietary milk preparations. These mild cases must be differentiated from a group of infants with similar manifestations due to lowered digestive powers. The latter group is perhaps best appreciated if one reviews the early papers on the efficacy of acid milks by Marriott and Davidson,[18] Faber,[19] Brennemann,[20] and others. They demonstrated that diarrhea could often be checked within 48 hours with no other treatment than an acid milk. The problem in diagnosis in the mild cases was originally defined by Schloss[10] in 1920 in the following statement:

> These patients, rarely show a positive cutaneous reaction to cow's milk protein, and it is difficult to determine definitely whether the symptoms are really due to sensitization to the proteins of cow's milk or merely to disordered digestion or to abdominal bacterial action in the intestinal tract.

Accordingly, when mild cases of noninfectious diarrhea requiring treatment are encountered, the first trial diet should consist of a formula that is heated, acidified,

16. McQuarrie, I., and Ziegler, M. R.: Comparison of Nutritive Value of Mineral-Enriched Meat and Milk, Pediatrics **5**:210, 1950.

17. Glaser, J., and Johnstone, D. E.: Soy Bean Milk as a Substitute for Mammalian Milk in Early Infancy, Ann. Allergy **10**:433, 1952.

18. Marriott, W. M., and Davidson, L. T.: Acidified Whole Milk as a Routine Infant Food, J. A. M. A. **81**:2007, 1923.

19. Faber, H. K.: Hydrochloric Acid in Infant Feeding, Am. J. Dis. Child. **26**:401, 1923.

20. Brennemann, J.: The Curd and the Buffer in Infant Feeding, J. A. M. A. **92**:364, 1929.

high in protein, and low in fat and carbohydrate. A successful result, in all likelihood, indicates that the infant has a functional lowering of digestive powers and not milk allergy. Exceptions to this statement are based on the fact that prolonged heating of milk reduces its anaphylactogenic powers. In this respect Ratner [21] sensitized animals to pure lactalbumin from raw milk and was unable to shock them with heated milk, whereas animals sensitized with heated milks could be shocked with lactalbumin from raw milk. Acidification of milk does not reduce its antigenic properties, as only the casein portion is curded and thus impeded from entering the intestinal tract in a soluble form. The liberated whey proteins lactalbumin and lactoglobulin, believed chiefly responsible for milk sensitivity, are easily accessible for absorption into the blood stream. Additional foods should temporarily be discontinued until a diagnosis is made, as hyperacidity probably retards absorption of allergens other than milk and the opposite state may occur with hypoacidity.[22] If the response to the high protein acid formula is unsatisfactory, milk allergy may be suspected. Two forms of treatment have been successfully employed. The first consists simply in a quantitative reduction in the amount of milk to the point of tolerance and completing the nutritional requirements with other foods. The second is the use of breast milk, goat's milk, and the hypoallergenic formulas. Additional articles of food should be introduced gradually and the child carefully observed for any allergic manifestations. Spontaneous recovery may occur at any time and is often erroneously attributed to the most recent change in formula. Oral desensitization is less commonly attempted today because of the availability of a large number of food substitutes. When successful, it permits the early return to a simple diet with a cow's milk formula.

The second group, comprised of infants with chronic diarrhea after the first year of life, was described in the early editions of the Griffith and Mitchell [23] textbook of pediatrics as cases of "mucous disease." This term, referring to the large quantities of mucus in the stools, originated with the description by Eustace Smith [24] in 1869 of a chronic form of diarrhea in children. The term was subsequently discarded in favor of such designations as "chronic gastritis," "mild or near celiacs," "intestinal catarrh," "steatorrhea associated with intestinal allergy," "steatorrhea associated with upper respiratory infections," and "chronic intestinal indigestion." The clinical picture of this variously named group of cases has many features in common and in general simulates true celiac disease both in the age of onset and in physical findings. What was thought to be an attack of acute diarrhea fails to improve or after a short remission again recurs. The frequency in the number of stools forms the initial complaint. The stools are loose, offensive, and often coated with mucus. As the disease progresses there is loss of weight, an enlargement of the abdomen, and flabbiness of the musculature. Frequently, the nasal mucosa is boggy gray in appearance, and long strings of mucoid nasal discharge appear during

21. Ratner, B.: The Treatment of Milk Allergy and Its Basic Principles, J. A. M. A. **105**:934, 1935.

22. Walzer, M.: Factors Influencing the Absorption of Allergens and Their Significance in Symptomatology and Treatment, J. Pediat. **21**:121, 1942.

23. Griffith, J. P. C., and Mitchell, A. G.: Diseases of Infants and Children, Ed. 2, Philadelphia, W. B. Saunders Company, 1937, p. 587.

24. Smith, E.: On the Wasting Diseases of Infants and Children, Philadelphia, Henry C. Lea, 1870, p. 183.

crying spells. Enlargement of the adenoids and redness of the tonsils are common findings. There is often a history of food intolerance during the early months of life. In the mild cases the babies may show no physical abnormalities. The report by Kunstadter[25] in 1943 more firmly established the role of food allergy as a cause of this disorder. His first case represents a typical example.

A male infant, aged 19 months, was breast fed up to 4 months of age and then given a dilute cow's milk formula. Sensitivity to certain vegetables, as evident by a rash, was the only sign of food intolerance. At one year of age he developed a diarrhea associated with a maculopapular rash. There was a watery discharge from the nose. On boiled skimmed milk, banana, and scraped apple the diarrhea stopped, but attempts to add various foods caused a recurrence. At 16 months of age he had four to seven foul-smelling mushy stools daily with a great deal of abdominal distention in spite of a diet consisting of boiled skimmed milk with Casec (calcium caseinate), ripe banana, lean beef, lamb, low fat cottage cheese, Jello, and vitamin supplement. Between the ages of 1 year and 17 months he lost 4 lb. (1,810 gm.); his abdomen became greatly distended; he was irritable, anorexic, and pale. No anemia was present. His appearance was typical of a child with celiac disease. Stool cultures and blood agglutination tests were unrevealing. The stools contained an increased amount of fat. Intracutaneous tests to milk, wheat, and eggs were negative. He was placed on a celiac diet with powdered protein milk, banana, meat, and Jello. He refused the protein milk and became constipated for the first time in several months. A recurrence of diarrhea followed the introduction of boiled skimmed milk. Cow's milk was again discontinued, and the stools became normal. He was able to tolerate soy bean milk and a fairly complete diet. Two months later he had gained 5 lb. (2,270 gm.), the abdominal distention had receded, and otherwise he appeared normal.

A similar group of cases was described by McKhann, Spector, and Meserve.[26] Both reports corroborate the earlier observations of Rowe.[27] No evidence exists to implicate food allergy as a causative factor in true celiac disease. Rickets and glossitis may develop in prolonged cases despite oral administration of vitamins. The role of the gastrointestinal tract in conditioning deficiency disease has been discussed by Strauss[28] in respect not only to vitamin lack but also to macrocytic anemias. The erroneous diagnosis of an intestinal infection in this group is often based on the dramatic cessation of diarrhea following the use of the sulfonamides or other chemotherapeutic agents. That this is purely a secondary effect due to the change in intestinal flora is evident by the invariable recurrence of diarrhea when the treatment is prolonged, the drug discontinued, or the dosage reduced. Vitamin deficiency from excessive antibiotic therapy plus the additional effects of anorexia, vomiting, and diarrhea resulting in a decrease in the production of B complex vitamins[28a] and vitamin K may complicate the picture. Stool analyses of fat content,

25. Kunstadter, R. H.: Gastrointestinal Allergy and the Celiac Syndrome, J. Pediat. **21**: 193, 1942.

26. McKhann, C. F.; Spector, S., and Meserve, E. R.: An Association of Gastrointestinal Allergy with the Celiac Syndrome, J. Pediat. **22**:362, 1943.

27. Rowe, A. H.: Food Allergy: Its Manifestations, Diagnosis and Treatment, with a General Discussion of Bronchial Asthma, Philadelphia, Lea and Febiger, 1932.

28. Strauss, M. B.: The Rôle of the Gastro-Intestinal Tract in Conditioning Deficiency Disease: Significance of Digestion and Absorption in Pernicious Anemia, Pellagra and "Alcoholic" and Other Forms of Polyneuritis, J. A. M. A. **103**:1, 1934.

28a. Diarrhea due to folic acid deficiency following the prolonged use of poorly absorbed sulfonamides is similar to the experimental folic acid deficiency described by Waisman, H. A., and others: Am. J. Dis. Child. **83**:398, 1952. Two personally observed cases of intestinal allergy treated with sulfonamides irregularly for many months were apparently complicated by folic acid deficiency. The diarrhea ceased abruptly after administration of this vitamin, recurred in one case when it was discontinued, and responded immediately to readministration of folic acid.

vitamin A absorption curves, and glucose tolerance curves are not diagnostically helpful. The defect in the absorptive capacity of the intestinal mucosa is thought to be due to the development of edema plus the increase in intestinal motility. The diarrhea may be differentiated from pancreatic disease by enzyme determination and from true celiac disease by a therapeutic trial on a strict celiac diet such as outlined by Howland.[29] Additional aid in the diagnosis of intestinal allergy by sigmoidoscopic visualization of localized areas of mucosal edema resembling wheals has been described by Lapin and Weissberg.[30] Other causes of chronic diarrhea at this age are rare and include tuberculous enteritis, chronic ulcerative colitis, mycotic infections, amebiasis, and other parasitic infections, regional ileitis, congenital intestinal malformations, multiple polyposis, and direct invasion of the intestines and mesenteric nodes with malignant tumors (lymphosarcoma and Hodgkins disease). The condition termed postdysenteric intestinal irritability has multiple causes for the persistence of diarrhea following bacteriologic cure and includes temporary impairment of digestive powers, true achlorhydria, colitis secondary to the use of antibiotics, deficiency of the B group vitamins, newly acquired food allergy, and psychogenic factors. Well-documented cases of chronic diarrhea of psychogenic origin in this age group do not appear in the pediatric literature. Pica may cause chronic diarrhea, depending on the type of foreign material ingested. "Starch intolerance" remains a controversial entity. Cases of intestinal allergy may show an excess of undigested fat and starch as demonstrated by stool emulsions stained with Sudan IV and Lugol's iodine.[7a]

When the above causes of diarrhea are excluded as well as possible by suitable clinical and laboratory observations the diagnosis again becomes narrowed down to a differentiation between food allergy and a functional impairment of the digestive powers. Inasmuch as neither diagnosis can be established unequivocally, a trial diet is justified. Success following a bland diet with part or all of the following components is fairly good evidence that the diarrhea is not allergic in origin: a low fat and carbohydrate content, absence of foods that are naturally laxative, an acid milk (low fat buttermilk), and supplements of hydrochloric acid, pancreatin, and vitamins. Although elimination diets in the treatment of food allergy have been criticized as a hit-or-miss method it may be said that, in general, success is directly proportional to the time expended in obtaining a careful history and to the proper analysis of the events that follow each change in diet. Standardized elimination diets (cereal-free, fruit-free, etc.) should be employed only in the absence of any help from the history and after a trial omission of the common offenders, milk, egg, wheat, orange juice, and fish oil. Of particular importance and not sufficiently stressed is the need to withhold, if possible, all major food substitutes until the intestinal irritability has subsided for fear that new allergies might be acquired. A case in point is that of a 2-month-old baby with a severe allergic diarrhea of the type described by Rubin.[9] A trial of soy bean milk was unsuccessful. One year later soy bean milk was again tried because of a mild recurrence of diarrhea. Following the ingestion of only 2 oz. (57 gm.), the child vomited repeatedly for six hours. The soy bean milk was

29. Howland, J.: Prolonged Intolerance to Carbohydrates, Tr. Am. Pediat. Soc. **33**:11, 1921.

30. Lapin, J. H., and Weissberg, W. W.: Sigmoidoscopy in the Diagnosis of Allergic Colitis, Am. J. Dis. Child. **76**:78, 1948.

discontinued and no additional symptoms occurred. Hill [31] has demonstrated in a group of eczematous infants with skin tests positive to cow's milk and with clinical improvement or cures following the removal of cow's milk that the substitution of soy bean during a time when there were apparently no intestinal disturbances resulted in skin tests positive to soy bean after a four-week interval but no clinical manifestations. The soy bean was introduced between the fifth to eighth month of life and it is apparent that age as well as the condition of the intestinal tract are factors in the acquisition of new food sensitivities of clinical significance. Essential in the elimination diet is a synthetic multivitamin preparation in an aqueous dispersion. One must carefully avoid the mild intestinal disturbances that occasionally follow overdosage of B-complex vitamins. The elimination diet may of necessity be inadequate for a short time, as it is important in the severe cases to postpone, temporarily, the use of major substitutes, reduce the fat content, and omit foods that are naturally laxative. Thus a trial diet for an infant during the second year of life suspected of allergy to dairy products would consist of a single grain cereal, preferably rice to which a small amount of juice from a can of pears may be added, banana, unsweetened applesauce, lean meat, potato, plain boiled rice, a vitamin supplement, and weak tea sweetened with saccharin. If successful, a milk substitute [32] may be added within 7 to 14 days. Other foods are given singly and the amount gradually increased until it is certain that a quantitative factor responsible for symptoms does not exist. This conservative regimen, not always necessary, will reduce the number of failures. Increases in the quantity of foods, especially the hypoallergenic milks, must be gradual, for if the point of tolerance is exceeded much valuable time is lost. The gradual reintroduction of the offending foods after an interval of three to six months is usually successful in this age group. Drugs are rarely necessary; antihistamines are not of value, and bismuth, paregoric, sulfonamides and antibiotics will often mask symptoms and delay diagnosis. There is a tendency for the diarrhea to subside spontaneously at about 2 years of age.

The prevention of food allergy has received serious consideration. Ratner [21] and Shannon [33] have advocated dietary restrictions during pregnancy to prevent hypersensitiveness in the offspring. Intrauterine sensitization, produced experimentally in guinea pigs, remains a controversial subject. Some reported cases in humans may represent sensitization after birth by antigens in the mothers' milk, and both Walzer [5] and Zohn [34] were unable to demonstrate any effect from the ingestion of excessive amounts of certain foods during pregnancy as judged by intracutaneous and passive transfer tests. Sufficient evidence does exist to justify restriction of the maternal diet in families with highly sensitive allergic individuals. By the same

31. Hill, L. W.: The Production of Nonetiological Skin Hypersensitivity to Foods by Natural Means in Atopic Persons, J. Allergy **13**:366, 1942.

32. Safe dilutions for the initial feedings with milk substitutes are as follows: Nutramigen, 8 tbsp. (120 ml.) to 1 qt. (8,000 ml.) of water; Mull-Soy, 6 oz. (180 ml.) to 26 oz. (770 ml.) of water; evaporated goat's milk, 6 oz. to 26 oz. of water; meat formula, strained beef, 100 gm., dextrose, 30 gm., water 32 oz. (950 ml.). Calcium and other minerals should be added gradually to the meat formula.

33. Shannon, W. R.: Eczema in Breast Fed Infants as a Result of Sensitization to Foods in the Mother's Dietary, Am. J. Dis. Child. **23**:392, 1922.

34. Zohn, B.: The Relationship of Maternal Diet to Intrauterine Sensitization, J. Allergy **13**:153, 1942.

reasoning the diet of the nursing mother under similar circumstances should not contain unboiled milk or an overabundance of any one food. That this is not an entirely theoretical conclusion is illustrated by Lyon's [35] well-substantiated case of severe allergy in a 3-week-old breast-fed infant due to the excessive ingestion of white navy beans by the mother. Similar cases have been described by Talbot [36] and by Shannon.[33]

Sensitization through the gastrointestinal tract during the early weeks of life undoubtedly represents the commonest source of food allergy, and if breast milk is not available, unboiled milk should not be used. The premature introduction of additional articles of diet, an unfortunate modern trend, should be avoided. The general plan of feeding outlined by Shulman [37] appears a reasonable one to follow. Kunstadter's [25] case illustrates that breast milk may simply delay the appearance of cow's milk allergy but not necessarily prevent it. This, however, is of the greatest importance as judged by the mortality of diarrhea in respect to age. As previously mentioned, the routine use of a milk substitute for normal newborn babies was attempted by Glaser and Johnstone.[17] Their percentage of failures or intolerance to soy bean milk appears too high to make this a worthwhile routine procedure. The routine use of a hypoallergenic milk during convalescence from diarrhea is not advocated by Darrow.[8] He believes that an acquired allergic state under such circumstances does not occur with sufficient frequency to justify this type of diet. Nevertheless Schloss's [3] original observation that foreign proteins are absorbed in unchanged form to a greater degree in infants with debility or any form of gastroenteritis suggests that the use of a milk substitute, for at least a short interval, may be of value in the presence of a bloody diarrhea and in very small infants with severe intestinal irritation. Any recommendations for a routine prophylaxis against food allergy remain questionable as long as the incidence of this disorder is unknown and in view of the tendency of the great majority of infants to thrive on almost any reasonable regimen.

436 N. Roxbury Dr.

35. Lyon, G. M.: Allergy in an Infant of 3 Weeks: Report of Case and Comment, Am. J. Dis. Child. **36**:1012, 1928.

36. Talbot, F. B.: Eczema in Childhood, M. Clin. North America **1**:985, 1918.

37. Shulman, M. H.: Prophylaxis Against Allergy: Pediatric Program, New England J. Med. **239**:391, 1948.

Abstracts from Current Literature

Metabolism; Infant Feeding; Milk and Other Foods

Treatment of Enterocolitis Due to Dysentery in Infancy. Angel Ballabriga, Arch. pediat. **2**:169 (Sept.) 1950.

The author reviews the causes of dysentery in various countries as reported. The treatment of dysentery due to Shigella and Flexner type bacilli is outlined. The drug of preference is "6257," which is a combination of formaldehyde and sulfathiazole with the trade name of Formacibazol. In cases in which there are secondary invaders which are Gram-positive sulfadiazine and sulfamerazine are used in conjunction with Formacibazol. Penicillin may also be used.

If there are infections due to the typhoid or paratyphoid type of organism, chloramphenicol (Chloromycetin) is the drug of first choice, but the author has had excellent results with Formacibazol when the antibiotic was not available.

The electrolyte balance must be maintained by saline, glucose, amino acid, Ringer's solution, etc. In the pediatric clinic in Barcelona, with which Dr. Ballabriga is associated, human plasma or the plasma of Masson is frequently used. The latter is a calf plasma which has had the anaphylactic characteristics reduced. It is given because of the fact that it has given no ill effects and is cheaper than human plasma. A cortical hormone of the adrenal gland (25 to 50 mg.) is added if the child shows symptoms of adrenal insufficiency.

In diet, carob bean flour in protein milk is given at first with addition later of bananas, scraped apples, and carrots.

In cases of less serious diarrheas the insoluble sulfonamides, such as sulfaguanidine, may be effective, but they should not be expected to do the work of antibiotics or Formacibazol.

Allen, San Francisco.

The Significance of the Use of Enriched Flour in the Diet. Beulah D. Westerman and Miriam Stone, J. Nutrition **44**:313 (June 11) 1951.

The reported experiments have produced further evidence of the beneficial effect of enriching flour. The significance of the use of enriched flour has been tested by feeding rats a combination of natural foods similar to those consumed by human beings. Measurements of growth through two generations were made, and reproduction and lactation performances were studied.

Fredeen, Kansas City, Mo.

Utilization and Protein-Sparing Action of Fructose in Man. Anthony A. Albanese, William C. Felch, Reginald A. Higgons, Betty L. Vestal, and Loukia Stephanson. Metabolism **1**:20 (Jan.) 1952.

The authors compared the utilization of glucose and fructose in two separate groups of subjects. In the first group (consisting of five fasting convalescent men) the blood level and urinary output of total sugars and of fructose were measured during and after intravenous infusion of 10% glucose and 10% fructose. The results obtained suggested that intravenously administered fructose is more readily metabolized than is administered glucose. Urine losses of "total sugars" were considerably greater during and after glucose infusion than were losses of "total sugars" during fructose infusion.

In the second group (consisting of four normally growing children aged between 7 and 12 years) nitrogen retention was measured while the subjects were ingesting diets which were of constant composition except for their carbohydrate contents. To simulate nutritional circumstances prevailing during parenteral carbohydrate alimentation, the diets were designed to supply normal gross amounts of protein per day but low percentages of protein calories and high percentages of carbohydrate calories. Total dietary carbohydrate was not varied, but the percentage of total carbohydrate made up of fructose, glucose, and galactose was changed

over one to four dietary periods. Nitrogen retention (expressed as nitrogen ingested minus nitrogen lost in the excreta) was always greatest when the percentage quantity of fructose was increased, even up to 70% of the total carbohydrate ingested.

The advantages of fructose over glucose administration at adequate levels of nitrogen intake are listed. They include more rapid utilization of fructose, greater protein-sparing effect, less tendency toward hyperglycemia (and the subsequent hypoglycemic rebound), and less tendency toward diuresis accompanying loss of urine sugar.

KAPLAN, Cincinnati.

NUTRITIONAL QUALITY OF MILK THERMALLY MODIFIED TO REDUCE REACTION. R. M. TOMARELLI, ELIZABETH LINDEN, and F. W. BERNHART, Pediatrics **91**:89 (Jan.) 1952.

Rat growth experiments have demonstrated that the impairment of the nutritional quality of milk by the heat treatment required for the preparation of a hypoallergenic product is a result of a destruction of vitamins. Young rats fed heat-treated milk fortified with minerals and all the usual vitamins with the exception of vitamin B_{12} grow at a suboptimal rate. The addition of liver powder or of a vitamin mixture containing vitamin B_{12} to the heat-treated milk results in a growth rate equal to that of rats fed unheated milk.

FROM THE AUTHORS' SUMMARY.

VARIATIONS IN THE PANNICULUS ADIPOSUS EUTROPHIC AND DISTROPHIC OBTAINED BY A NEW MICROMETRIC METHOD. VENERANDO CORRENTI, Arch. ital. pediat. e puericolt. **14**:119, 1950.

The author reports the results of his investigations on the variations in the thickness of subcutaneous fat layer in eutrophic and in dystrophic children, aged from 3 to 30 months. After having enumerated the previous investigations and the methods applied, he notes the importance given by other authors to the latter for the evaluation of the nutritional status. He describes his own new technique in micrometric measurement by means of an instrument modified by himself, which he has called *maiachistometro* (measurer of soft tissues). The measurements were made in eight different regions and they were repeated after lapses of time varying from 6 to 43 days; the investigation periods lasted from 6 to 205 days. The findings were statistically analyzed.

From the results obtained, considered by the author only as indicative because of the not too large number of the cases investigated, the following deductions may be drawn: The subcutaneous fat layer in eutrophic infants seems to be distributed in the various areas according to an established scheme, which very often shows a remarkable regularity. The dystrophic status greatly disturbs the distribution of the subcutaneous fat layer, which tends to recover the normal aspect as soon as health is returning.

FROM THE AUTHOR'S SUMMARY.

A SPECIALLY MODIFIED WHOLE MILK FOR INFANTS. L. MARTONI, Clin. pediat. **33**:277 (May) 1951.

The author discusses a milk powder preparations, Pontolac, in which cow's milk has been modified to simulate the composition of human milk—with lower casein content and 60% of the fats unsaturated—which was found to be well absorbed and tolerated by normal and by undernourished infants. With some infants, loose bowel movements were replaced by stools of normal consistency.

HIGGINS, Boston.

ACTION OF BONE MEAL ON THE GROWTH OF DYSTROPHIC INFANTS. D. GOTTI and P. NICOLAJ, Clin. pediat. **33**:291 (May) 1951.

Dystrophic infants showed remarkable gains in weight following the addition to the feeding of 0.40 gm. of bone meal daily. The supplement used was Ossipan, a preparation from the whole bone of young animals. The opinion is expressed that the gains in weight were due not so much to the mineral components as to some enzymes and hormones.

HIGGINS, Boston.

CLINICAL AND THERAPEUTIC INDICATIONS FOR THE USE OF A TONIC CONTAINING AMINO ACID RADICALS. G. MARTINI, Minerva pediat. **4**:461 (June 15) 1952.

A proprietary product, Aminoiodoarsolo, containing iodine, arsenic, cobalt, histidine, and glutamic acid, was given intramuscularly as a tonic to 27 debilitated and anemic children. Excellent results are reported, as shown by an improvement in appetite, a gain in body weight, and increased hemoglobin and red blood cell count.

HIGGINS, Boston.

ACUTE NUTRITIONAL DISTURBANCES IN INFANTS IN AN ASYLUM. WERNER BUSTAMANTE E. and JOSE LEGARRETA, Rev. chil. pediat. **20**:437 (Oct.) 1949.

The authors studied the characteristics of the acute nutritional disturbance in a group of 71 babies from the Asylum Section of the Children's Hospital "Luis Calvo Mackenna," who have been under continual medical control for the first 12 months of life.

Eighty-three cases of acute nutritional disturbances, including two cases of toxicosis, are presented. Age, season, nutritional status, type of feeding, and evolution are compared in cases of enteral and of parenteral origin.

Escherichia coli was present in almost every stool culture. The mortality rate from 1942 to 1948 was very low in this section, and the low rate confirms the importance of the preventive medical care.

FROM THE AUTHORS' SUMMARY.

INFANT FEEDING IN A WELFARE SERVICE. ERNESTO FIGUEROA R., Rev. chilena pediat. **22**:381 (Sept.) 1951.

Infantile feeding in a welfare service that has control over many children must not be guided by local and restricted criteria, but must consider the national characteristics in addition to the peculiarities of metabolism in children. To achieve this goal, the pediatrician must work in close collaboration with experts on social economy, nutrition, and public health.

AUTHOR'S SUMMARY.

"HALTUNSVERFALL" OF SCHOOL CHILDREN IN CONSEQUENCE OF HUNGER. HELMUT BOEHNCKE and ERICH BRINKMANN, Med. Wehnschr. **76**:972 (Aug. 3) 1951.

"Haltungsverfall" is an acute deterioration of body posture. A weak rounded back is the most prominent sign. These children do not respond properly to normal physical and mental demands. This *Haltungsverfall* has become more frequent during the past years. It is especially noteworthy that as a rule a spurt in length precedes it, with a disproportion of the growth in weight.

AMBERG, Rochester, Minn.

THE VALUE OF PROTEINS AND PROTEIN HYDROLYSATES IN UNDERNOURISHED CHILDREN. J. HNATEK and J. SVEJCAR, Pediat. Listy **6**:92, 1951.

Eighty infants, 50 of whom suffered from very severe forms of diarrhea (11 from severe wasting [atrophy] and the rest from dystrophy) were fed with Pronotrin, an enzymatically digested casein (mixture of amino acids and polypeptides). The infants tolerated the hydrolysates well; in only 12% of the cases did the treatment have to be interrupted because of vomiting independent of the treatment. In this way it became possible to increase in these infants the amount of proteins with hydrolysates to 15 gm. per kilogram of body weight daily. The average increase in weight amounted to 32 gm. daily in the atrophic children and to 53 in the diarrheic patients during the first seven days of realimentation. The authors conclude that the amino acid requirement of these patients is much higher than that of normal infants and also that the requirement of normal infants is higher than it was thought to be. To obtain rapid realimentation of undernourished children it is preferable to use protein hydrolysates rather than proteins because of the lowered ability to digest proteins, of which these children need an extraordinarily high amount.

FROM THE AUTHORS' SUMMARY.

THE TIME FACTOR IN THE METABOLISM OF BIOTIN IN VARIOUS DISEASES, PARTICULARLY LIVER DISEASES. R. GOSTOV and J. RIMAN, Pediat. listy **7**:204, 1952.

The authors studied the metabolism of biotin in infectious hepatitis. Excretion in the urine was increased in the early phases of the disease; during regression it fell to deficiency values and later returned to normal. If regression did not occur, the loss of biotin remained high, particularly in conditions of a progressive character, e. g., cirrhosis of the liver. Isolated investigations in other diseases showed similar changes.

FROM THE AUTHORS' SUMMARY.

STUDIES ON PLACENTAL PERMEABILITY WITH RADIOACTIVE ISOTOPES OF PHOSPHORUS AND IRON. J. NAESLUND, Acta obst. et gynec. scandinav. **30**:231, 1951.

Radioactive phosphorus (P^{32}) and radioactive iron (Fe^{59}) were injected into the mother's circulation from 10 to 90 minutes before delivery. In the study with radioactive phosphorus, consisting of 6 previously reported and 13 new experiments, in one there was a considerably higher specific radioactivity in the child's blood cells than in the child's plasma or maternal blood, suggesting that some of the mother's radioactive blood corpuscles entered the fetal vascular system. All the remaining experiments with radioactive phosphorus were negative, the child's blood corpuscles containing little if any specific radioactivity, the values obtained being lower than in the maternal plasma. Seven experiments were made with Fe^{59}. In four of the seven experiments the child's blood cells showed a fairly high specific radioactivity, while there was hardly any in the child's or the mother's plasma. The results of these experiments suggest the likelihood that some of the mother's radioactive blood corpuscles had entered the fetal vessels.

DANFORTH, Evanston, Ill.

THE RELATION OF BREAST FEEDING PROGNOSIS TO THE INITIAL AMOUNT OF MATERNAL MILK. GERT V. SYDOW, Acta Pediat. **41**:449 (Sept.) 1952.

In a series of 1,836 consecutive cases of infants with a birth weight of 3,000 gm. or more, who had not shown any manifest defects during the first week of life and who after discharge with their mothers to their homes could be followed at least to the age of 2 months, the duration of breast feeding was compared with the amount of milk produced by the mother on the infant's sixth day of life. Duration of breast feeding was reckoned as the total time until the infant was definitely weaned from the breast. Those infants whose mothers had delivered 200 ml. of milk or less on the sixth day had considerably shorter periods of breast feeding than the rest, 44.1% being weaned before 2 months of age against 6.6 to 0.6% in the other groups, and only 22.1% being breast-fed for at least six months, as against 50 to 80% in the groups with higher initial lactation. In cases in which the mother had been able to pump out at least 100 ml. of milk beyond what the infant had sucked, the infant was breast-fed for a considerably longer time than the mean of the total series; this applies both to infants who had been able to suck at least 300 ml. as well as to infants who had sucked not more than 200 ml. It seems possible therefore, to improve the prognosis of breast feeding in many cases by regular manual emptying of the breast.

FROM THE AUTHOR'S SUMMARY.

Vitamins; Avitaminoses

RIBOFLAVIN IN HUMAN SERUM. K. SUVARNAKICH, G. V. MANN, and F. J. STARE, J. Nutrition **47**:105 (May 10) 1952.

Suvarnakich and his colleagues investigated the riboflavin content of normal human serum. In 141 normal well-nourished persons, free serum riboflavin and flavin-adenine-dinucleotide were 0.84 ± 0.71 and 2.32 ± 0.42 γ per 100 cc., respectively. There were no differences between sexes and age groups. Serum riboflavin values, especially for flavin-adenine-dinucleotide, should be of value in the diagnosis of human riboflavin deficiency.

FREDEEN, Kansas City, Mo.

INFANTILE SCURVY. A. D. PACKER, Clin. Rep. Adelaide Children's Hosp. **1**:66 (Nov.) 1947.

The cases of four children with scurvy admitted within six months are described.

McGUIGAN, Evanston, Ill.

RADIOLOGICAL SIGNS IN RICKETS AND THEIR DIFFERENTIAL DIAGNOSIS. J. N. BERRY, Indian J. Pediat. **19**:110 (July) 1952.

The classic diagnostic roentgenological findings in rickets are described. Points to be considered in differential diagnosis include physiological cupping of the lower ends of the radius and ulna; growth lines; lead, phosphorus, and bismuth lines; congenital syphilis; scurvy; osteogenesis imperfecta; hyperparathyroidism, and renal osteodystrophy.

McGUIGAN, Evanston, Ill.

DEFICIENCY OF PANTHOTHENIC ACID. A. GIROUD, Études néo-natales **1**:5 (Feb.) 1952.

A survey was made of the various maternal deficiencies and their consequences, and an experimental study of pantothenic acid deficiency was made.

In birds, this deficiency exerts an influence on the reproductive function. In rats, if experimented on from the 16th to the 23rd day before mating or on the very day of mating, it causes a defect of the implantation of the ovum, fetal resorption, and abnormally reduced litter.

A description of the synthetic diet is given. Control was carried out by means of vaginal smears and weight curves of the pregnant rats; they were killed on the 21st day of gestation; fetal resorption was observed if deprivation had been started before mating (10 to 30 days); if it had been started before 3 to 10 days, abortion and congenital anomalies ensued: exencephalus, pseudocephalus (cerebral tissue is indistinguishable); anophthalmos or microphthalmos (symmetrical or dyssymmetrical); hemorrhages of the extremities, and subcutaneous edema. Control animals were normal, and the supplementing of pantothenic acid prevented the development of defects.

FROM THE AUTHOR'S SUMMARY.

VITAMIN B_{12} IN CHRONIC NUTRITIONAL DISTURBANCES. M. LATO and O. BISCATTI, Lattante **23**:484 (Aug.) 1952.

Ten dystrophic infants were given intramuscularly 10 γ of vitamin B_{12} daily for 20 days. Each of the children showed improvement under the treatment, having gained in weight and having increase in the number of reticulocytes. Dystrophy is believed to be due to deficiency of the B vitamins, from either poor absorption or insufficient intake, and especially of the B_{12} vitamin.

HIGGINS, Boston.

ABSORPTION OF WATER-SOLUBLE VITAMIN A. A. MASI and G. P. MAZZETTI, Riv. clin. pediat. **48**:685 (Nov.) 1950.

The authors report on the hematic and hepatic levels of vitamin A in guinea pigs after the injection of the water-soluble vitamin preparation into the blood stream. Results show the opposite behavior of the hematic and hepatic levels produced by the injections. The authors also report a series of data relative to the storage of vitamin A in the liver after the intramuscular injection of water-soluble preparations.

They point out that water-soluble vitamin A, whether introduced into the blood stream or into the muscular tissues, is rapidly and completely absorbed and stored in the liver.

FROM THE AUTHORS' SUMMARY.

CRITICAL REMARKS CONCERNING TREATMENT WITH VITAMIN T GOETSCH. J. HARZHEIM, Deutsche med. Wchnschr. **76**:1019 (Aug. 17) 1951.

It is emphasized that in order to determine the value of T-vitamin for the gain in weight of infants it is necessary to maintain constant nutritional conditions. Fifteen infants, thirteen of whom were dystrophic, were treated with the vitamin. No definite result became evident. In the five cases studied no stimulation of the bone marrow was noted.

AMBERG, Rochester, Minn.

EXAMINATION OF EPITHELIUM FOR LATENT VITAMIN A DEFICIENCY AND BEGINNING KERATOMALACIA IN INFANTS. H. BRUGSCH, Ztschr. Kinderh. **68**:267, 1950.

Since determinations of vitamin A in the blood are inadequate for the determination of vitamin A deficiencies in infants, Brugsch searched for a more practical test. Similar to examinations of epithelial scrapings in rats, which are accurate enough to be used for potency determinations of vitamin A preparations, the author describes the examination of vaginal scrapings of infants as an equally reliable test. In order to apply this test also to male infants, the results of examinations of rectal scrapings were compared with those of vaginal examinations and found equally reliable. The changes indicating vitamin A deficiency and responding to vitamin A therapy are the presence of epithelial cells without nuclei and of cornified cells and the absence of leucocytes.

GLASER, Jerusalem.

REPORT ON FOUR YEAR STUDIES ON RICKETS. GERT VON SYDOW, Svenska Läk.-tidning. **49**:957 (April) 1952.

Experiences from the north of Sweden are reported. It is maintained that from October to May no infants are exposed to ultraviolet sun rays. It is suggested that in addition to the deficiency of vitamin D there is some other factor responsible for the development of rickets. Boys acquired rickets more often and earlier than girls, and infants who had acquired rickets were markedly somatically underdeveloped. The author believes that these other factors in the development of rickets are of a genetic character.

WALLGREN, Stockholm, Sweden.

A HALF-CENTURY OF CHILD HYGIENE. E. GORTER, Maandschr. kindergeneesk. **20**:1 (Feb.) 1952.

Three cases of rickets are reported. One is that of a child who never was given vitamin D and lived in a house where the sun never entered the living rooms. The mother was unable to take the child outdoors or to visit a physician. The other two patients were refractory to any treatment. One of these never had more than 3 mg. of phosphorus per 100 cc. of blood; the other had normal values. The next observation concerned an infant 4 months of age, who presented edema after a mild intestinal disorder. Hypoproteinemia accounted for the edema. The importance of the study of proteins in pediatrics is stressed.

FROM THE AUTHOR'S SUMMARY.

Hygiene; Growth and Nutrition; Public Health

THE ROLE OF THE PHYSICIAN IN THE SCHOOL HEALTH PROGRAM. R. L. SIMMONS, New Orleans M. & S. J. **104**:574 (Aug.) 1952.

The importance of the school health program is stressed. One of the basic objectives of this program is the development of a relationship between the physician and the families he serves who have school age children. This relationship will enable the families to receive the specific medical guidance that may be indicated on an individual basis and under conditions that will promote the intelligent use of the physician throughout adult life as well as the school years. This is a planned educational project, and physicians of a community should have detailed knowledge of and cooperate wholeheartedly with the school health program.

McGUIGAN, Evanston, Ill.

STATISTICS ON MORTALITY RATE IN CHILVICOY, ARGENTINA, DURING THE PERIOD 1941-1945. Arch. argent. de pediat. **38**:230 (Oct.) 1947.

The mortality due to pregnancy and labor is high. The fact that the mortality due to nutrition deficiency ranks above that due to other causes labels this part of the country as a zone with deficient sanitary services.

ROJAS, Boston.

THE NECESSITY IN URUGUAY OF ORGANIZING MEDICAL PEDAGOGICAL ASSISTANCE TO THE STUDENT WITH DEFECTIVE HEARING. CARLOS A. BAUZA, Arch. pediat. uruguay **21**:889 (Nov.) 1950.

The use of pure tone audiometry as a means of diagnosing the type of hearing loss as well as of testing hearing acuity for tones of high frequency, as indication of hearing damage due to tubal pathology, is a necessity for school health examinations in Uruguay.

The hearing loss disturbs the psychological adjustment of the school child and interferes with his scholastic achievement; this is often mistakenly interpreted as feeble-mindedness.

Uruguayan statistics point out the existence of 15.2% of school children with some degree of hearing loss. Approximately 5% of them have a hearing loss so severe as to interfere with speech hearing.

In agreement with several otologists and teachers of Uruguay, the authors recommend the creation of special classes for hard-of-hearing children, led by specialized teachers, and with the help of the electroacoustical science.

A medical prophylactic and pedagogic plan can be successful only through close cooperation among the health authorities, school authorities, and the school children and their families.

FROM THE AUTHOR'S SUMMARY.

SCHOOL SOCIAL WELFARE WORK FOR A SOCIALLY ADJUSTED NATION. BLANCA A. CASSAGNE SERRES, Bol. Inst. internac. am. protec. infancia **23**:251 (Sept.) 1949.

In view of the benefits that social welfare work brings to the individual and to society, Cassagne Serres proposes that the Second Provincial Social Service Congress recommend (1) that the benefits of social welfare work be extended to all Argentine school children; (2) that teachers and professors be interested in the social application of the organization of these services in the schools, and (3) that programs of pedagogy for normal schools include some fundamental subjects related to social welfare work, especially those that are related to the formation of human personality.

FROM THE AUTHOR'S CONCLUSIONS.

INFLUENCE OF MALNUTRITION UPON BODY WEIGHT AND SIZE OF CHILDREN OF SCHLESWIG-HOLSTEIN IN THE POST-WAR PERIOD. W. DROESE and E. ROMINGER, Ztschr. Kinderh. **67**:615, 1950.

A statistical evaluation is presented of length and weight of children of various age groups in the years 1945 to 1948. Infant growth was retarded in 1945, but infant mortality was not affected. In 1946 the weight gain in infants raised on mixed feeding improved. No influence of the better food conditions could be noticed upon purely breast-fed infants. In older children the results of malnutrition were noticed later (1946) and affected weight more than length (10% and 4%, respectively). In large cities a partial or total regain of the body weight was noted in 1947; the length remained below average. In small cities weight and length were regained. The authors explain this difference in recovery by the fact that the increased caloric intake in the large cities consisted of carbohydrate and vegetable protein, whereas in the small cities a higher quality food of fat and animal protein was sufficiently available, especially for small children in whom the best recovery could be noted.

KURT GLASER, M.D., Jerusalem.

THE ORGANIZATION OF NEWBORN'S DEPARTMENTS: THE ORGANIZATION OF WORK. J. POHLAVA, Pediat. listy **6**:172, 1951.

The pediatricians' and nurses' work in the infants' wards is described on the basis of personal experience. Their work consists essentially of curative and preventative duties, education, administration, and cooperation with the obstetrician.

GRULEE, Evanston, Ill.

HOW A CHILD GUIDANCE CLINIC WORKS. ELSA-BRITA NORDLUND, Acta pædiat. **38**:517, 1949.

The author tells how a child-guidance clinic connected with a hospital (the Norrtull Hospital, Stockholm) functions.

FROM THE AUTHOR'S SUMMARY.

Hospital Admissions. J. H. P. Jonix, Maandschr. v. kindergeneesk. **17**:131, 1949.

Jonxis discusses the frequency of admissions to the Children's ward of the Zuiderziekenhuis (Rotterdam) since its opening, 10 years ago. This frequency is greatly dependent on the social conditions in which the parents of the children are living. A ward for convalescents has been of great importance, especially with respect to the problem of the treatment of the children who belong to the social lower levels.

From the Author's Summary.

Prematurity and Congenital Deformities

A New Roentgen Sign of Fetal Death. Stephen Nathaniel Tager, Radiology **67**:106 (Jan.) 1952.

Previously described signs of fetal death evident on the roentgenogram are (1) overlapping the bones of the cranial vault; (2) flattening of the vault; (3) asymmetry of the skull; (4) marked curvature or angulation of the spine; (5) indistinct bone markings; (6) failure of the fetus to change position; (7) collapse of the thoracic cage; (8) halo of the skull due to separation of the skin from the skull, and (9) gas in the fetal circulatory systems, heart, abdominal vessels, and umbilical cord.

The author describes three cases in which fetal death was recognized because of the collapse of the fetal spine. Roentgenograms of the mother are made in the erect and in the supine position. In the erect position, there is complete collapse of the fetal spine. In these three cases, overlapping of the bones of the cranial vault was not present.

Hodgson, Rochester, Minn.

Can Morquio's Disease Be Differentiated From Gargoylism as a Disease Sui Generis? O. Aegler, Ann. Pediat. **176**:159 (March 1951.

The author describes two typical cases of early gargoylism with quantitative and qualitative reduction of the carpal bones. Typical cases of early and of late gargoylism and of Brailsford-Morquio disease are compared and difficulties of differential diagnosis explained, particularly for x-ray diagnosis. The three clinical pictures are understood to be three different types of the same pleiotropical recessive-inheritable disease in which the differences consist only in the intensity of the symptoms and in the age at which they manifest themselves.

From the Author's Summary.

Statistics on Illegitamacy and Prematurity. F. Rasi and E. Drago, Rev. clin. pediat. **51**:392 (Feb.) 1953.

The authors, having drawn attention to the high percentage of immature children born of illegal unions, publish the corresponding statistics for immature children at the Provincial Institute of Assistance to Infancy at Padua from 1947 to the end of 1951. They suggest that these institutes—the only ones organized for nourishment of infants with human milk on a paid basis—should adapt their equipment for the assistance of legitimate immature infants.

From the Authors' Summary.

Prematurity and the Use of Vitamin E. Ascencion Ariz Elcarte, Acta pediat. españ. **94**:1161 (Oct.) 1950.

Elcarte presents five cases of severe prematurity in which she used vitamin E preparations along with the other vitamin preparations and other modalities used in the treatment of prematurity including the incubator, oxygen, ultraviolet, and estrogens. In these five cases the gain in weight was noticeably faster than in cases in which only A and D, etc., were given. In some cases in which a child has merely been able to hold his own for two or three months, the addition of vitamin E caused marked increase in weight and general maturity.

The form of vitamin E used was a capsule of Evion (10 mg.) and in cases in which both A and D were given with vitamin E, the product called For Vitem was used. This was given only once a week, since it contains 250,000 units of vitamin A, 500,000 units of vitamin D and

30 mm. of vitamin E. Both were tolerated by mouth. In other cases, 10 mg. of Evion was given daily. In two cases Evion alone was used and the babies gained weight and did as well as the others receiving massive doses

The author discusses the characteristics of the premature infant as to poor development of heat regulation, poor capillary development in lungs, lazy or absent sucking reflexes, poor tolerance of fats, etc., and says she does not know the reason for this characteristic of vitamin E unless it is stimulation of growth in the cells and tissues.

None of the premature infants weighed more than 2,500 gm. and one weighed 2,100 gm. All were clinically extremely weak and given to attacks of cyanosis.

ALLEN, San Francisco.

THE SIGNIFICANCE OF GOETSCH'S VITAMIN T COMPLEX FOR THE GROWTH OF PREMATURE INFANTS. HEINZ POTOSCHNIG, Med. Klin. **46**:987 (Sept. 14) 1951.

The complex "T" is obtained from a yeast (Torula utilis). The preparation was given by mouth to a number of premature infants of 1.3 to 2.3 kg. birthweight. Growth in weight and length exceeded expectation.

AMBERG, Rochester, Minn.

BONNEVIE-ULLRICH SYNDROME. K. B. STARKE, Monatsschr. Kinderh. **98**:420 (Oct.) 1950.

The cases of four infants and children with Bonnevie-Ullrich syndrome are reported. The most important of the congenital anomalies were cranial nerve defects, mammillary dysplasia, skeletal muscle defects, ptosis of the eyelids, lymphangiectatic edema of the hands and feet, and webbed neck. Other abnormalities noted in some of the patients were epicanthus, high and narrow palate, retrognathia, mental retardation, asymmetry of the external ears, subluxation of the hips, ankylosis of joints, clubfoot, and cutaneous nevi. There was no family history of such congenital defects in any of the cases.

HARTENSTEIN, MILWAUKEE.

DYSOSTOSIS CLEIDOCRANIALIS. J. RICHARD, Acta paediat. belg. **6**:79, 1952.

A typical case is described clinically; roentgenograms are demonstrated, and the literature is reviewed.

GLASER, Jerusalem.

VITAMIN B_1 IN PREMATURE INFANTS. R. GOSTOF and B. RASKA, Pediat. listy **6**:158, 1951.

The level of thiamine (vitamin B_1) in the cerebrospinal fluid of 22 premature babies was found to be lower than that generally accepted as normal for full-term newborn infants and infants. Most of the babies in whom the vitamin was absent or present in traces only either died or were in a very bad general condition. The authors consider this fact to indicate parenteral administration of thiamine hydrochloride in combination with other components of the vitamin B complex to premature infants. The influence of thiamine on the metabolism is discussed.

GRULEE, Evanston, Ill.

KLIPPEL-FEIL SYNDROME FROM A HETEROSPECIFIC PREGNANCY. E. KRATKOVA, Pediat. listy **6**:352, 1950.

A case of Klippel-Feil syndrome with hydrocephalus, meningocele, and Arnold-Chiari syndrome from a heterospecific pregnancy is described. The most likely etiologic agent of these multiple malformations may be the incompatibility of Rh system. The antigen titer of the mother was negative the whole time. The author points out the possibility of congenital malformations from heterospecific pregnancies in a positive anamnesis even with a negative antigen titer.

FROM THE AUTHOR'S SUMMARY.

MORTALITY AMONG PREMATURE INFANTS. PER SELANDER, Acta pædiat. **38**:571, 1949.

The author suggests some lines along which data concerning premature babies should be arranged and worked up in order to permit comparisons between materials from different centers. Mention is made of Crosse's data from Birmingham as a model worthy of being followed.

A comparison between her series of cases and a series from a Swedish provincial hospital shows that the premature mortality which plays so important a part in infant mortality should be lowered by energetic measures during the second to seventh days of life.

FROM THE AUTHOR'S SUMMARY.

PHACOMATOSIS IN THE KLIPPEL-TRÉNAUNAY SYNDROME. W. G. SILLEVIS SMITT and W. A. VAANDRAGER, Maandschr. kindergeneesk. **18**:389, 1950.

A clinical survey is given of the four best known phacomatoses, viz.: Lindau-von Hippel disease, Sturge-Weber disease, Recklinghausen's neurofibromatosis, and tuberous sclerosis, so far as these concern pediatrics.

Two less known phacomatoses are also discussed, Albright's disease and the syndrome of Klippel-Trénaunay, both recognized as starting during infancy.

An extensive case history of a little girl with the Klippel-Trénaunay syndrome is given.

In view of the etiological factors concerned, it is important to mention that the patient's family history shows several cases of endocrine disturbance.

FROM THE AUTHORS' SUMMARY.

RETROLENTAL FIBROPLASIA IN HOLLAND. C. H. O. M. VON WINNING, Maandschr. kindergeneesk. **20**:268 (Sept.) 1952.

Thirty cases of retrolental fibroplasia are now known to have occurred in the Netherlands. The development of the eye disease is described in two of them. New concepts concerning the etiology and treatment are discussed, and the urgency for ophthalmological follow-up of premature babies is once more stressed, the more so since the new and promising oxygen therapy has been introduced.

FROM THE AUTHOR'S SUMMARY.

Newborn

ROOMING-IN OF MOTHER AND BABY IN HOSPITAL. JOHN C. MONTGOMERY, Illinois M. J. **102**:191 (Sept.) 1952.

Montgomery presents a general discussion of the advantages and disadvantages of rooming-in of mother and baby in the hospital.

BARBOUR, Peoria, Ill.

REACTIVITY OF THE SKIN OF THE NEWBORN INFANT. ABE MATHESON, MARVIN NIERENBERG, and JOSEPH GREENGARD, Pediatrics **10**:181 (Aug.) 1952.

The skin of the full-term newborn infant reacts to various dilutions of histamine phosphate with erythema but no wheal formation, as contrasted with the skin of older children, in which with the same technique (scratch) whealing was frequent.

The skin of the full-term newborn infant is capable of fixing reagin locally. Similar fixation of antibody (and skin reactions with a tendency toward smaller wheals) was shown in prematurely born infants of varying ages and weight.

The skin sites passively sensitized with serum containing reagin to egg showed erythema and whealing following the feeding of whole raw egg to both newborn infants and older children. This suggests that proteins or products of protein digestion, of sufficient complexity to be antigenic, are absorbed from the gastrointestinal tract of both newborn infants and older children.

This study supports the view that the skin of the newborn infant is capable of demonstrating an antigen-antibody reaction and that such reaction may be in the nature of erythema or whealing.

FROM THE AUTHORS' SUMMARY.

PROTHROMBIN AND ACCELERATOR GLOBULIN IN THE PLASMA OF NEWBORN INFANTS UNDER NORMAL AND PATHOLOGICAL CONDITIONS. S. VAN CREVELD, P. PAULSSEN, and S. K. TENG, Études néo-natales **1**:87 (Dec.) 1952.

The concentration of prothrombin and plasma accelerator-globulin was determined by means of the two-stage method of Ware and Seegers in (1) Healthy newborn infants, full-term and

premature infants, and healthy children between the ages of one month and one year; (2) several infants with so-called intrauterine melena neonatorum, and (3) an infant with severe congenital liver disease caused by an adenosis of the liver.

Results obtained by the authors with the two-stage method confirm the existence of a marked hypoprothrombinemia directly after birth, the prothrombin level being lower in premature infants than in full-term infants. The decrease of the prothrombin level in the newborn infant takes place on the second day of life and is approximately equal in the two groups of newborn infants. The level rises slowly again from the third day of life onward and reaches values on the seventh day of life which are only slightly higher than those on the first day. It takes about a year before the prothrombin level in infants has reached the same values as in older children and adults.

Administration of vitamin K directly after birth and for the first four days does not raise the prothrombin level to values found in older children and adults. On the other hand, vitamin K can prevent the fall of the prothrombin level on the second day of life.

The concentration of the plasma accelerator-globulin was normal in full-term and premature infants at birth and showed no changes.

In three cases of so-called intrauterine melena neonatorum the authors found a physiological hypoprothrombinemia, which was not severer than that found in healthy newborn infants. Apart from this hypoprothrombinemia, low levels of plasma accelerator-globulin were found. The authors conclude from these findings that the combination of a low prothrombin level and a low concentration of plasma accelerator-globulin may be the cause of melena.

In a rare case of adenosis of the liver, a combined deficiency in both clotting factors was found seven weeks after birth. Whereas the plasma accelerated-globulin in this case soon rose to a normal value, the prothrombin content of the plasma, after a temporary increase, progressively decreased till the death of the child.

FROM THE AUTHORS' SUMMARY.

HYPOTONIAS OF NEWBORN INFANTS. ANDRE THOMAS and SAINT-ANNE-DARGASSIES, Études néo-natales **1**:115 (Dec.) 1952.

Muscle tone is peculiar in the newborn infant as compared with the adult. It is about the same in the seven-month premature as in the full-term infant, with the exception of laxity of the head. In both premature and full-term infants there is an anatomical and developmental sign which demonstrates that the motor part of the cortex does not play a role in the control of the tonus; in the premature infant, the pyramidal tract is not present, and in the full-term infant it is not yet myelinated. Therefore, in the newborn period, hypotonia does not have its origin in a pyramidal lesion. Bilateral mild hypotonias are not very significant.

Of greater importance is the discrepancy between permanent tonus of the upper limbs and tonus of the lower limbs (double obstetrical paralysis of the brachial plexus, hypotonia of the legs caused by spina bifida).

The most important hypotonias are observed in the very small premature infants, with intracranial hemorrhages, obstetrical trauma, in mongolism, Foerster's syndrome, or Werdnig-Hoffmann paralysis, and in some with coexisting edema or cyanosis.

In itself, bilateral hypotonia is not always of immediate prognostic value; in mild cases, separation of the normal from the abnormal is somewhat difficult. Isolated or combined, hemihypotonia is of a greater clinical importance; it means a definite organic, sometimes permanent, disturbance.

In partial hypotonia, bone or muscle conditions should always be checked. At birth, it is almost impossible to be sure of a cortical lesion; such an involvement is diagnosed at the time of functional development. Rigidity must be correctly interpreted; it is often difficult to recognize whether it is of pallidal or pyramidal type. Rigidity does not exclude the possibility of a reduction of the permanent tonus (mainly hyperextensivity). The prognosis of hypotonias is also discussed.

FROM THE AUTHORS' SUMMARY.

INCOMPLETE COLD ANTIBODIES AS THE CAUSE OF ANTIGLOBULIN TESTS IN THE NEWBORN CHILD. L. HOLLANDER, Helvet. paediat. acta **7**:512 (Nov.) 1952.

In a Rh-positive newborn baby, an antiglobulin test was positive. In the serum of the mother no blood-group-specific immune antibodies were present. The erythrocytes were sensitized with incomplete cold antibodies. It can be assumed that these kinds of antibodies were transmitted to the baby by diaplacental route.

FROM THE AUTHOR'S SUMMARY.

ANOXIC SYNDROME OF THE NEWBORN. JESUS MARTINEZ FERNANDEZ, Acta pediat. españ. **8**:1201 (Oct.) 1950.

Dr. Fernandez reviews the mechanism of normal respirations and enumerates the pathological conditions which may embarrass respirations in the newborn. The lack of oxygen in a newborn infant is much more serious because of the labile nature of the respiratory center.

The number of conditions which may affect the respiration are numerous and may be classified as (1) respiratory, (2) circulatory, (3) hematic, (4) cellular, (5) nervous system.

Among respiratory conditions are included all congenital anomalies of larynx, bronchi, bronchioles, and alveoli, and also lesions affecting the thoracic wall, such as congenital amyotonia. Besides congenital anomalies, the presence of blood and mucus in the respiratory organs may interfere with the normal exchange of oxygen and carbon dioxide.

Under circulatory lesions the various congenital cardiopathies are discussed. Uterine tetany, hemorrhage, placental separation, prolapse of the cord, long labor, etc., may interfere with proper oxygenation of the blood and indirectly with respiration. After birth, hemorrhage, blood dycrasias, and severe anemias may embarrass respiration indirectly, also.

Injuries to the nervous system incident to birth may affect the respiratory center, and the improper use of drugs before and immediately after birth may accentuate the anoxic state.

The author includes a schematic drawing of "Schreiber's wheel" to show these various relations.

The treatment is prevention, removal of cause, artificial respiration, oxygen tents, aspiration of mucus, and, where indicated, transfusions, antianemic drugs, and vitamin K both before and after delivery.

Naturally, the prolonged anoxia may cause convulsions, spastic and mentally retarded children and/or death.

ALLEN, San Francisco.

NEWBORN DEPARTMENT OF THE CLINIC FOR THE CARE OF BABIES PRAGUE-PODOLI. KAMIL KUBAT, Pediat. listy **4**:200, 1949.

The newborn department in Prague-Podoli, which is part of the baby clinic and of the third maternity clinic, is described. The baby clinic has other departments: the sick baby department (40 beds), and the premature baby department (20 beds). It is characteristic that the pediatric service is permanent. The pediatrician checks daily on all the babies and takes charge of the newborn immediately after birth. The cooperation of obstetrician and pediatrician is here particularly close and fruitful. The department has 110 cots situated in 15 rooms. The babies' room is placed between two rooms for mothers and holds 4 to 12 cots. Equipment and internal arrangement of the babies' rooms are described, as well as the main principles of organization of the department. The pediatric nurses attend the children and work under the sole direction of the pediatrician. One nurse looks after 12 babies during an 8-hour work period. The ratio, one nurse to four babies (for 24 hours), is the same day and night. All babies and mothers are examined for Rh factor and BCG vaccinated. Great importance is given to the education of mothers and popularization of breast feeding. Visits of relatives are not allowed in the department. Only one baby is christened at a time, and in the presence of the father and godfather only. Premature babies have their own department, as do babies suspected or known to be sick. The department has preventive and curative, as well as educational and scientific, duties, directed principally at lowering newborn mortality.

FROM THE AUTHOR'S SUMMARY.

THE ORGANIZATION OF NEWBORN DEPARTMENTS: V. RESUSCITATION OF ASPHYXIATED INFANTS. K. ZNAMENACEK, Pediat. listy **6**:177, 1951.

Resuscitation by means of insufflation of oxygen into the lungs and the general resuscitation plan successfully employed at the institute of care for mothers and infants are described.

GRULEE, Evanston, Ill.

PECTUS EXCAVATUM CONGENITUM. V. KAFKA and J. SALEK, Pediat listy **7**:267, 1952.

Four cases of pectus excavatum congenitum in children 3½ to 12 years old are reported in which operations by the method of Brown or Ravitch, according to the degree of the depression, were carried out. The surgical treatment of pectus excavatum underwent substantial changes in consequence of Brown's anatomical and physiological studies elucidating its formal genesis. Thereby, the indication for surgical intervention have been put on a new basis. The changes concern the kind, the extent, and the proper time of the operation. The report points out the advisability of the surgical treatment in infancy (under 2 years) as a preventive procedure. Further, it describes the evolution of the surgical treatment of pectus excavatum and its new methods and deals with the clinical features of pectus excavatum, its complications, and the indications for operation.

FROM THE AUTHORS' SUMMARY.

AIR-BORNE INFECTIONS IN THE NEWBORN. K. ZNAMENACEK and E. ALDOVA, Pediat. listy **7**:321 (Dec.) 1952.

The characteristics of a neonatal department are described from the point of view of air-borne infections, and the results of the authors' first attempt to follow them are summarized. The finding that beta hemolytic Streptococcus is not of clinical importance for the newborn infants, who are at the same time defenseless against some types of Staphylococcus aureus, makes it necessary that the research of the bacterial flora in relation to the reactivity of the neonatal organism be intensified and that the microbiological technique for typing strains of the Staph. aureus be extended. Around this organism will be concentrated the fight for the purposeful prevention of air-borne infections in neonatal departments.

FROM THE AUTHORS' SUMMARY.

A CASE OF PERFORATIONS OF THE INTESTINE IN A NEWBORN INFANT. L. M. J. VAN DRIEL, Maandschrift kindergeneesk. **21**:177 (June) 1953.

After a study of the literature a survey is given of the clinical features and the etiology of perforations of the bowel in newborn infants. A new case of perforation of the cecum in a stillborn child is described. The primary alteration was a chronic inflammatory process of the terminal ileum and of the whole of the ascending colon, as evidenced by a thickening of the submucosa and subserosa, in which mononuclear infiltration cells were found. The process must have originated in intrauterine life. The etiology remained completely obscure.

FROM THE AUTHORS' SUMMARY.

Acute Contagious Diseases

RELATION OF SEX, PREGNANCY, AND MENSTRUATION TO SUSCEPTIBILITY IN POLIOMYELITIS. LOUIS WEINSTEIN, W. LLOYD AYCOCK, and ROY F. FEEMSTER, New England J. Med. **245**:54 (July 12) 1951.

The authors studied 108 women between the ages of 20 and 40 with poliomyelitis who were admitted to the Haynes Memorial Hospital, Boston, in 1949 and 1950. The number of pregnant women in this group was three times greater than that expected by coincidence, although even when this was statistically accounted for there were still more women than men with poliomyelitis.

From the clinical observations made during this period it is concluded that pregnancy, probably through the alteration of intricate endocrine gland mechanisms, increases susceptibility

to clinical poliomyelitis. Two features are important, (1) that possibly the host is made more susceptible to initial invasion by the virus, and (2) that subclinical invasions may be more easily converted to nervous system involvements.

It is postulated that pregnancy may alter not only susceptibility, but also the course of the preexisting infection. Evidence is presented to show that parturition may increase or initiate muscular involvement. Either changes in smooth muscle physiology by exertion or rapidly altered endocrine balances may be etiologic features in the latter phenomenon.

Finally, it is suggested that there is a point in the menstrual cycle (about 12 days prior to the onset of menses) wherein susceptibility to poliomyelitis is enhanced.

The apparent role of sex, pregnancy, and menstruation in increasing susceptibility in the adult reemphasizes the possible influence of the sex hormones or other endocrine substances on the pathogenesis of this disease.

WHEELOCK, Denver.

ARTERIAL HYPERTENSION ASSOCIATED WITH ACUTE ANTERIOR POLIOMYELITIS. FLETCHER H. MCDOWELL and FRED PLUM, New England J. Med. **245**:241 (Aug. 16) 1951.

Arterial hypertension, with a diastolic blood pressure greater than 90, appeared in 45 of 95 adolescents and adults with acute anterior poliomyelitis. Males were twice as frequently affected with hypertension as were females.

The highest incidence of hypertension occurred in patients suffering bulbospinal paralysis of all four extremities; in 29 of the 30 patients requiring artificial respiration arterial hypertension developed.

The blood pressure in hypertensive patients not requiring artificial respiration averaged 143/96, and lasted a mean of 5.5 days.

The blood pressure in hypertensive respirator patients surviving the acute stage of the disease averaged 164/104. The hypertension of these patients has already lasted an average of 98 days, and 10 patients still have hypertension, 3 to 12 months after the onset of their illness.

The appearance of artificial hypertension in these patients may have been the result of invasion of brain-stem autonomic structures by poliomyelitis virus or may have been a manifestation of a generalized alarm reaction. Anoxemia, hypercapnia, or artificial respiration appeared to intensify and prolong the otherwise transient hypertensive state that occurred.

FROM THE AUTHORS' SUMMARY.

EXPERIMENTAL PRODUCTION OF POST-TONSILLECTOMY BULBAR POLIOMYELITIS. HAROLD K. FABER, ROBERT C. MCNAUGHT, ROSALIE J. SILVERBERG, and L. DONG, Proc. Soc. Exper. Biol. & Med. **77**:532 (July) 1951.

Poliomyelitis occurring within 30 days after tonsillectomy is predominantly bulbar. The authors removed the tonsils of cynomolgus monkeys by enucleation with curved scissors (1) immediately after application of virus to the pharnyx, and (2) three days after inoculation of virus into the thalamus. In a control series, virus was swabbed on the surface of the mouth and pharynx but tonsillectomy was not done. In all experiments a 17% suspension of the Wis 1945 strain (Brunnhilde type) of poliomyelitis virus, PD_{50} 4.9, was used. All monkeys previously were prepared by division of the olfactory tracts to preclude entry of infection through the olfactory nerves. After 7 to 10 days, primary bulbar paralysis accompanied less often by high spinal paralysis was found in the animals whose tonsils had been enucleated. Intrathalamic inoculation of virus followed three days later by tonsillectomy was regularly followed within two more days by bulbospinal paralysis in which all levels of the cord were involved. After oropharyngeal swabbing with virus without tonsillectomy, spinal paralysis usually resulted, with bulbar manifestations in only one instance. When there was pharyngeal application of virus followed by application of 2% tincture of iodine and then by tonsillectomy, all animals (6) remained well.

HANSEN, Galveston, Texas.

IMMUNIZATION IN INFANCY. G. E. WHITE, Canad. M. A. J. **67**:658 (Dec.) 1952.

Routine immunizations of infancy are outlined. The procedures recommended follow closely the recommendations of the American Academy of Pediatrics.

MCGUIGAN, Evanston, Ill.

STUDIES IN POLIOMYELITIS. V. MEASROCH, J. GEAR, and G. I. FAERBER, South African M. J. **25**:421 (June 23) 1951.

The authors studied nine healthy infants at monthly intervals for evidence of infection with poliomyelitis and of Coxsackie-like virus in the stools without having had evidence of illness. A year previously 3 of 16 babies in the same group had been shown to have poliomyelitis virus in the stools, and a silent infection.

McGUIGAN, Evanston, Ill.

A PROCEDURE FOR BIOLOGIC DIAGNOSIS BY DEMONSTRATING THE VIRUS IN THE MENINGEAL FORMS OF POLIOMYELITIS. LOUIS-ANDRE MARTIN, JEANNE DELON, JACQUES GREVIN, LUCIEN CATALA, and JOSETTE FELIX, Presse méd. **56**:1170 (Sept. 6) 1952.

It is established that hitherto no certainty has been brought about by the laboratory into the diagnosis of nonparalytic poliomyelitis. The virus has been demonstrated in the monkey, but with material difficulties and practically insurmountable cost. It has also been found in the mouse, but in one variety only (Lansing's variety). Since G. Blanc and L. A. Martin in 1948 had shown the rabbit to be susceptible to the poliomyelitis virus, the writers attempted to use this animal for inoculations to prove the presence of the virus in the feces and blood of those patients for whom the etiologic diagnosis cannot be established through the clinical signs, which is the case in the meningeal forms of poliomyelitis. They give full report of 8 cases in which it was possible to isolate a virus capable of serial passage to the rabbit. The poliomyelitic nature of the virus was demonstrated either by crossed immunity tests with those viruses well known and kept up in the laboratory, or by a neutralizing action of an in vitro mixture with an antipoliomyelitis serum.

FROM THE AUTHORS' SUMMARY.

FIRST OBSERVATIONS ON THE ACTION OF SYNTHETIC ANTI-HISTAMINES IN THE EXANTHEMEIC DISEASES OF CHILDHOOD. R. CORDA, Ann. ital. pediat **4**:155 (April) 1951.

The author has observed the administration of antihistaminic drugs in some exanthematous diseases of children (measles, scarlet fever). The therapeutic results obtained (milder course, shortening of exanthematic period, etc.) confirm the possibility that the antihistaminic drugs may be a valuable therapeutic help for measles and especially scarlet fever.

GRULEE, Evanston, Ill.

FEVER THERAPY IN POLIOMYELITIS. P. PINNA and A. RACUGNO, Ann. ital. pediat. **4**:212 (June) 1951.

The authors in the Cagliari Pediatric Clinic examined the prophylactic therapeutic possibilities of spontaneous and induced malarialization with regard to the paralytic manifestations of Heine-Medin disease (acute anterior poliomyelitis).

From the numerous case reports their conclusions were mostly negative and such as to make this method inadvisable because of its rather serious inconveniences.

Better but not quite conclusive results were observed at the institution with pyretotherapy with sulfurated substances and chiefly with polyvalent vaccine suspensions.

The authors believe that, in these reactions, there are complex reactive elements, cellular, humoral, and nervous, but that their influence is limited to activating and accelerating the functional revival of medullar cells.

FROM THE AUTHORS' SUMMARY.

THE SPINAL FLUID IN VARICELLA. PAOLA PALA, Ann. ital. **5**:430 (Oct.) 1952.

The author examined the behavior of the cerebrospinal fluid in 30 children affected by varicella without clear nervous onsets. After stating something about clinical and fluid alterations that may occur during the nervous complications of varicella, he reports the data of examinations made both at the beginning and the regressive period of the disease, through which pressure and sugar appear increased.

Such alterations show a very little disturbance of the nervous system and of blood-fluid barrier and show conditions in which, for several causes, nervous onsets, may appear. The examination of cerebrospinal fluid might, in such cases, give useful indications.

FROM THE AUTHOR'S SUMMARY.

PHENOLSUFATHIAZOLE AS AN ANTIBIOTIC IN EXPERIMENTAL POLIOMYELITIS. D. GOTTI, Clin. pediat. **31**:631 (Nov.) 1949.

Clinical observations were made in experimentally induced poliomyelitis in cats. In some cases the phenolsulfathiazole (Darvisol) was given by mouth before the inoculation, in some cases at the time of the inoculation and in others after the appearance of the symptoms of the disease. The conclusion is drawn that the drug was without appreciable beneficial results.

HIGGINS, Boston.

EPIDEMIOLOGICAL IMPORTANCE OF DIPHTHERIA CARRIERS. A. ROSA and R. OLIVO, Gior. mal. infect. e parassit. **4**:1 (Jan.) 1952.

Carriers are responsible for the persistence of diphtheria in a community. On the other hand, persons with immunity to diphtheria have doubtless at some time been carriers. A bibliography of 191 articles on diphtheria carriers is given.

HIGGINS, Boston.

ISOLATION OF THE VIRUS OF MUMPS. P. TOLENTINO and F. SEMACH, Gior. mal. infett. e parassit. **4**:305 (Nov.) 1952.

The authors have cultured on chick embryo a virus from a patient with mumps; the mumps was contracted during a remission of leukemia. The virus yielded a complement-deviation test with the sera of both the patient and other persons with mumps. The virus was not sensitive to either chloramphenicol or aureomycin.

HIGGINS, Boston.

THE LIPOID PHOSPHATE IN EXPERIMENTAL DIPHTHERITIC INTOXICATION: DIPHTHERITIC INTOXICATION AND THE LIPOID P CONTENT IN THE MYOCARDIUM OF THE RABBIT. F. CHEMI, Riv. clin. pediat. **47**:494 (July) 1949.

A reduction of the lipoid phosphate in the myocardium of guinea pigs treated with diphtheria toxin has been found by the author. Experimental proof is given that lecithin is able to delay the death of these animals caused by the toxin.

FROM THE AUTHOR'S SUMMARY.

AUREOMYCIN IN THE TREATMENT OF MALIGNANT DIPHTHERIA. ARRIGO GALEOTTI-FLORI and ROANO ROSSI, Riv. clin. pediat. **50**:21 (Jan.) 1952.

The authors have introduced aureomycin with satisfactory results in the therapy of malignant diphtheria. In experimental research on guinea pigs the authors propose a hypothesis regarding the therapeutic action of aureomycin and streptomycin in malignant diphtheria.

FROM THE AUTHORS' SUMMARY.

AMBULATORY TREATMENT WITH CHLOROMYCETIN IN A GROUP OF INFANTS WITH WHOOPING COUGH. JULIO MENEGHELLO R. and ARTURO GALLO B., Rev. chilena pediat. **22**:195 (May) 1951.

The authors report their studies on the ambulatory treatment of pertussis in children with chloramphenicol (Chloromycetin). They treated 37 children, with 15 control patients. All these were seen in the outpatient department and controlled every three days. Treatment consisted in a daily dose of 500 mg. for infants and 1 gm. for older children during a five-day period, followed by one-half the original dose for another five days. Although they recognize the difficulty of evaluating the results in the treatment of pertussis, they conclude that chloramphenicol is a useful drug in this disease, but that the criteria, the dosage, and the duration of treatment, must be reviewed to obtain better results. In many cases a decrease in frequency

and intensity of the paroxysms was evident 10 days after treatment was begun. Improvement in coughing was always accompanied by disappearance of vomiting, and anorexia and an improvement in the general condition of the child.

Nevertheless, these patients continued coughing for two months. In many cases there was a relapse after treatment was suspended, especially in those cases with only partial treatment.

FROM THE AUTHORS' SUMMARY.

TREATMENT OF MENINGOCOCCUS MENINGITIS. B. RAMOS, Arch. pediat. Uruguay **1**:49 (July) 1950.

The author outlines the treatment of meningitis of the epidemic type in which he used sulfadiazine and penicillin. Desoxycorticosterone (Percorten) with penicillin and sulfadiazine has been used with spectacular results in treatment of the Friderichsen-Waterhouse syndrome. This synthetic adrenal hormone may be used routinely, even when no gross hemorrhage of the adrenal gland is suspected.

ALLEN, San Francisco.

VACCINATION AGAINST WHOOPING COUGH. KARL-AXEL MELIN, Svenska läk.-tidning. **49**:1174 (May) 1952.

The author maintains that children with signs of diseases in the central nervous system should be excluded from whooping-cough vaccination because the vaccination in these children may produce a severer illness than the whooping cough itself.

WALLGREN, Stockholm, Sweden.

RISK FOR SUFFOCATION IN MEASLES ENCEPHALITIS. PER BENDZ and CARL-GUNNAR ENGSTRÖM, Svenska läk.-tidning. **49**:1768 (July) 1952.

A report is made on three children suffering from measles encephalitis with convulsions and unconsciousness, cyanosis, atonia, and apnea. During the convulsions large quantities of mucus in the bronchi produced an obstruction of the respiratory passages. By treatment of the children in the prone position with suction and oxygen, the danger of suffocation was successfully removed, and the children were discharged healthy.

WALLGREN, Stockholm, Sweden.

NEUROSURGERY AND THE TREATMENT OF ACUTE AND CHRONIC MENINNGITIS. H. VERBIEST, Maandschr. kindergeneesk. **18**:187, 1950.

In acute meningitis intrathecal administration may cause irritation of the meninges, while the antibiotic may not reach all foci of inflammation. In some patients there is ependymitis in one or two ventricles. For diagnosis and therapy ventricle puncture and drainage are necessary in those cases. After healing of the meningitis blindness and hydrocephalus may result. If blindness is caused by neuritis, nothing can be done. In a few cases, however, perineuritis is found; then surgical intervention may have success. In every case of blindness following meningitis exploration is justified. Treatment of hydrocephalus has not had good results. The operation of Matson was performed in one case. The patient died. In patients with tuberculous meningitis neurosurgical treatment must be instituted early. In most cases internal hydrocephalus develops at an early stage of the disease. Verbiest recommends ventricular puncture in every case of tuberculous meningitis as soon as the diagnosis is made. Hypertension in the ventricles is an indication to start ventricle drainage. Streptomycin must be administered intramuscularly, intrathecally, and intraventricularly.

In some cases of extensive basilar meningitis a cure can be achieved by drainage of the basilar cisternae and injection of streptomycin through the intracisternal drain.

VAN CREVELD, Amsterdam, Netherlands.

Acute Infectious Diseases

SODIUM GENTISATE IN THE TREATMENT OF RHEUMATIC DISEASE AND OF SCHOENLEIN-HENOCH PURPURA. S. PALESI, Clin. pediat. **35**:112 (Feb.) 1953.

Nine children, 6 to 12 years of age, 3 with Schoenlein's purpura and 6 with acute manifestations of rheumatic fever, were given daily doses of 3 to 8 gm. of sodium gentisate. The medicine was well tolerated, and in general the therapeutic results were good. However, the author feels that sodium salicylate is the preferable drug for use in these conditions, in that it seems to cause a greater antihyaluronidase action and to react to stimulate the adrenal cortex.

HIGGINS, Boston.

FIFTEEN SPORADIC CASES OF INFECTIOUS MONONUCLEOSIS. G. BELLONI, Gior. mal. infett. e parassit. **4**:363 (Nov.) 1952.

Of the 15 cases of infectious mononucleosis studied, 6 were in children and 9 in young adults; 8 occurred in the spring, 3 in the fall, 3 in the winter, and 1 in the summer. Eleven of the patients had prodromal symptoms, such as slight fever, headaches, and malaise, 3 to 13 days before the onset of the more acute symptoms of fever, pharyngitis, and adenitis. Eleven patients had splenomegaly, and 9 hepatomegaly. The Paul-Bunnell test was positive in only 6 of the patients. The white blood cell count was 13,300, with 24% granulocytes. The bone marrow was found to contribute to the hyperplasia of the reticuloendothelial cells.

The author believes that infectious mononucleosis is not a single disease or syndrome, but is caused by any of a number of lymphotrophic viruses.

HIGGINS, Boston.

INITIAL SYMPTOMS IN RHEUMATIC FEVER. ERIK JACOBSSON, Nord. med. **39**:1319 (July 9) 1948.

Jacobsson reviews the initial symptoms in 589 cases of rheumatic fever in children. In 69.5% of the total number of cases the illness began with pains in the joints; chorea was the first symptom in 17.7%, abdominal symptoms in 6.1%, subjective cardiac disturbances in 2.7% and signs of meningitis in 1.9% of the cases. Fever was the initial symptom in 64.7%.

WALLGREN, Stockholm, Sweden.

Chronic Infectious Diseases

TOXOPLASMOSIS. A. BALLABRIGA, Arch. pediat. **2**:19 (July) 1951.

The literature on toxoplasmosis is reviewed and three cases presented, not as case histories, but by comparison of symptoms and pathology with the classical findings in toxoplasmosis. The clinical diagnosis is made on the basis of (1) a progressive hydrocephaly which was initiated in fetal life, (2) the cerebral areas of calcification, and (3) ocular signs. In the latent form, there may be an acute febrile exanthematous illness with atypical pneumonia.

The hydrocephaly and the characteristics of the spinal fluid are described. Rarely is the parasite demonstrable in the spinal fluid. The fluid is xanthochromic and sanguinous with elevated albumin and few cells, but as the condition becomes chronic the spinal fluid appears more normal. However, animal inoculation gives rather typical findings with an abundance of organisms, pseudocystic lesions, etc.

The intracranial calcifications may be found by x-ray, but must be differentiated from tumors and other lesions. The calcification areas may be small or enormous and have a predilection for the areas at the level of the choroid plexus. In many cases with no calcification by x-ray there is definite evidence of calcification on autopsy studies. The ventricles may be enormously dilated.

The ocular signs may be microphthalmia; the areas of choroiditis may simulate a macular coloboma but, because of their irregular form and pigmentation, are typical. The lesions may also simulate congenital syphilis at a later stage. The eye examination is important because the pathology found in the chorioretinitis due to toxoplasmosis may appear much earlier than lesions in other parts of the nervous system. Many other lesions not pathognomonic for toxoplasmosis may be noted such as strabismus and nystagmus. If the child lives long enough, blindness ensues.

Besides the classical symptoms, neurological signs such as convulsions, spasticity, difficulty of swallowing, tremor of tongue, and choreiform and athetoid movements may confuse the diagnosis. Signs of liver damage and pulmonary invasion may be noticed.

The development may be acute and rapid, with blindness and mental deficiency, but a few patients have had evidences of old healed lesions and yet lived and maintained normal intelligence.

The differential diagnosis must be made between this and sarcosporidiosis.

The laboratory tests are described. The intradermal test must be carefully checked, as confusion with kala-azar is possible.

There is no specific treatment. In the cases reported sulfathiazole and intravenous ethylstibamine were administered because of intercurrent infections.

ALLEN, San Francisco.

ORGANIZATION AND FUNCTIONING OF A VACCINATION CENTER FOR BCG. R. A. MARQUEZY, Pédiatrie **38**:545, 1949.

Of the three methods of BCG vaccination, the author stresses the effectiveness of scarification, which produces no untoward complications. The oral method he rejects because of ineffectiveness, and the intradermal, because of the frequent formation of cold abscesses. He emphasizes the need for giving first a percutaneous and intracutaneous tuberculin test and for the strict separation before and after vaccination of children from a questionably or frankly contaminated environment.

The vaccination can be practiced in "closed" or "open" centers. The "closed" type receives children from tuberculous parents immediately after birth or older children with negative tuberculin reactions, vaccinates them, supervises their placement, and revaccinates them. The "open" centers see children three times. The first visit is for anamnesis, examination, fluoroscopy, and percutaneous test; the second visit, for reading of the percutaneous reaction and, if it is negative, administration of an intradermal test, and the third visit, if the test is negative, for vaccination. The children present themselves each year for retesting and revaccination if the test has become negative.

GLASER, JERUSALEM.

REGIONAL CENTER FOR ANTITUBERCULOUS VACCINATION IN GRENOBLE. L. BETHOUX, Pédiatrie **38**:551, 1949.

The author describes the functioning and results of the antituberculosis center in Grenoble, which consists of three pavilions: one for pregnant women with tuberculosis, one for newborn infants of tuberculous mothers, and one for older children of tuberculous parents. Oral BCG vaccination was practiced.

GLASER, JERUSALEM.

OBSERVATION ON THE ACTION OF STREPTOMYCIN IN TUBERCULOUS MENINGITIS. G. MACCIOTTA, Ann. ital. pediat. **4**:463 (Dec.) 1951.

The author gives the results of an experiment on therapy of tuberculous meningitis developed in the Pediatric Clinic of Cagliari with 87 observations (excluding those which lasted less than three days).

First, he tells the results already obtained in Italy and in other countries.

From the negative results of 1947 (treatment generally insufficient) the percentage of recovery (clinical and humoral) rose to 20% in 1948, to 25% in 1949, and to 29.5% in 1950, while the results already obtained (35.7%) and the great betterment of 1951 give hope that the last percentage may be maintained or even increased.

Recoveries date in one case from 41 months, in two from 36, in one from 33, in one from 30, in seven from about 2 years, and in eight from 3 to 14 months.

Nervous complications were less. These results were referred to the continual adjustment of treatment, to the clinical and spinal fluid conditions of each subject, to continuation of treatment after the patient had become normal for two months at least, and to the action of para-aminosalicylic acid and semicarbazone (by mouth).

The best results were obtained in pure meningitis and in pulmonary miliaric lesions; not so good results were obtained in forms with infiltrative lesions; negative results were obtained in encephalomeningitis.

Results might be bettered if the patient were admitted to the hospital earlier, but negative results are not always due to the time of the starting of treatment.

One should start with the average dose, and adjust the dosage to the individual patient.

Average intraspinal doses are 1 to 2.5 mg. per kilogram per day, with higher doses for younger children (in two administrations during the first 10 to 15 days and then in a single dose). Administration is stopped after two months as alterations in the spinal fluid suggest.

Average intramuscular doses 200 to 400 gm. per kilogram of weight, with a three to four day period each month without administration.

The author discusses the ways of introduction and their indication, the frequency of nervous complications, and the causes of failure.

FROM THE AUTHOR'S SUMMARY.

SURVEY OF A GROUP OF CHILDREN VACCINATED TWELVE YEARS PREVIOUSLY WITH PETRAGNINI'S ANATUBERCULIN. U. SALA, Clin. pediat. **35**:67 (Feb.) 1953.

The author has evaluated the status of 88 children who were vaccinated with Petragnini's anatuberculin as infants or very small children twelve years previously. No case of injury to the patient from the vaccination was found; a few had residual scars at the site of inoculation, but the scars were of minor significance. Only 13 of the children still had positive tuberculin reactions. Twenty-two of the children had died, only one from tuberculosis and the others from diseases occurring in early childhood, such as gastroenteritis, sepsis, or bronchopneumonia.

HIGGINS, Boston.

EARLY AND LATE RESULTS OF SEASHORE CLIMATE ON TUBERCULOUS CHILDREN. A. STEFANELLI, Clin. pediat. **35**:85 (Feb.) 1953.

A statistical and clinical review was made of the immediate and late results of the treatment of 800 tuberculous children at a sanatorium in a pine grove 150 yd. (137 m.) from the seashore. The results were excellent while the children were at the seashore, and the improvement continued after the discharge and the children had returned to their homes in the city and country.

HIGGINS, Boston.

IMPORTANCE OF PARAAMINOSALICYLIC ACID IN THE TREATMENT OF TUBERCULOUS MENINGITIS. G. PASQINUCCI and G. BARTOLOZZI, Riv. clin. pediat. **47**:434 (June) 1949.

Over 60 patients with tuberculous meningitis have been treated with *p*-aminosalicylic acid given by oral, rectal, intravenous, and intraspinal administration. The detailed data obtained will be given later; here, the result obtained in almost a year's research on tolerance according to the various ways of administration, on the blood and spinal fluid values are briefly stated. The importance of intraspinal therapy is stressed.

FROM THE AUTHORS' SUMMARY.

RESULTS FROM VIOMYCIN IN TUBERCULOSIS IN THE CHILD. ALVARO MASI and MARCELLO GIUSTI, Riv. clin. pediat. **49**:781 (Nov.) 1951.

The authors report the first clinical results of employment of viomycin associated with other drugs having an effect against tuberculosis, in tuberculosis and in particular in tuberculous meningitis of the child. Although the results obtained cannot be considered conclusive, owing to the short period of observation and the scarce quantity of the drug at their disposal, they have been up to the present rather good, and open the field to a wider application of this antibiotic especially in those forms which are not benefited by the combined use of streptomycin, paraaminosalicylic acid, and sulfone and in cases of streptomycin resistance.

FROM THE AUTHORS' SUMMARY.

STUDIES CONCERNING CLINIC, PATHOLOGY, SEROLOGY AND THERAPY OF CONGENITAL TOXOPLASMOSIS. HELMUT WEYERS, Arch. Kinderh. **142**:161, 1951.

Weyers discusses the literature, differential diagnosis, congenital and adult forms, and laboratory diagnosis of toxoplasmosis. Particularly the serological diagnosis and the diagnostic fallacies are carefully considered, and two observations are added.

GOTTSTEIN, Chicago.

THE LEIPZIG REGIME FOR PREVENTION AND TREATMENT OF CONGENITAL SYPHILIS. JOHANNES OEHEM, Deutsche med. Wchnschr. **35**:1024 (Aug. 29) 1952.

The regimen of treatment in the university clinic of Leipzig of 81 cases manifest congenital syphilis proved efficient for a two-year period of observation. In the dispensary, nearly 1,000 children of syphilitic mothers are watched. Of these, 250 have congenital syphilis. All the children of syphilitic mothers are examined carefully, and a serologic examination of the spinal fluid is made before dismissal. The treatment consists of one course of penicillin over 15 to 20 days. The serological reaction becomes negative three to four months after the start of the treatment without recurrence so far. The regimen is as follows: (*a*) Prevention of infection of the infant by penicillin treatment of the syphilitic mother, even though she has been syphilitic once and offers no signs. This preventive measure should be regulated by law. (*b*) One course of exclusive penicillin treatment in cases of congenital syphilis with a total of 400,000 international units per kilogram of body weight divided over two to three weeks. Young and school children first received penicillin treatment followed by combination with neoarsphenamine-antimony. (*c*) Preventive treatment after birth to the age of 6 months with penicillin, if the syphilitic mother has not been treated or insufficiently treated. Such safety measures were carried out in 92 infants, none of whom became syphilitic.

AMBERG, Rochester, Minn.

THE VEGETATIVE FUNCTIONS OF CHILDREN WITH TUBERCULOUS MENINGITIS DURING AND AFTER TREATMENT WITH STREPTOMYCIN AND CONTEBEN OR PARAAMINOSALICYLIC ACID. WALTER LEUTERER and GUTHER LUFT, Med. Klin. **46**:289 (March 9) 1951.

The vegetative functions of children with meningitis under treatment were tested with determinations of blood pressure, fasting blood sugar, and the response to the blood sugar curves to insulin and epinephrine. The meningitis itself may lead to an increase of blood pressure and of the fasting blood sugar as well as to aberration of the blood sugar curves on testing with insulin and epinephrine. When the meningitis became quiescent, a return to normal of all tests occurred usually. For further detail the paper is to be consulted.

AMBERG, Rochester, Minn.

TREATMENT OF TUBERCULOUS MENINGITIS WITH STREPTOMYCIN. HOEN, Monatsschr. Kinderh. **97**:190 (July) 1949.

Of 10 patients with tuberculous meningitis treated with streptomycin, 2 died, 1 was cured completely, while the other 7 are alive with some neurological disturbance. Schizophrenia developed in one patient during the course of treatment. Ages ranged from 3 to 14 years; two were female, and eight male. The longest duration of treatment so far had been 214 days. The author advises against intracisternal injection and advocates combined intraspinal and intramuscular routes of administration. Vestibular disturbances were not noted during streptomycin therapy. Morbilliform exanthemata occurred in two patients and disappeared as soon as use of streptomycin was discontinued. No evidence of renal damage was found. A daily intramuscular dose of 1 gm. is advised. Intraspinal dosage of 1 mg. per kilogram every other day, later every two to three days is thought to be sufficient. Early initiation of treatment is essential for success; somnolent or comatose patients have very little chance for improvement with therapy.

Generally, streptomycin seemed to prolong life for patients with tuberculous meningitis and convert the course of the disease from a rapidly fatal into a more chronic one.

HARTENSTEIN, Chicago.

TUBERCULIN SENSITIVITY AFTER BCG VACCINATION. GUENTER LATSCH, Montasschr. Kinderh. **98**:467 (Dec.) 1950.

Six hundred children who had received BCG became tuberculin-positive (Mantoux) 7 to 15 days later. After four weeks they reacted positively to 0.1 mg. of tuberculin and continued reacting positively to this dilution for the following five months. Higher sensitivity to tuberculin was found in children who had complications following BCG vaccination, in children who had had several BCG vaccinations, and in children who had a superimposed infection with virulent organisms occurring before, during, and after BCG vaccination. Positive reactions to 0.01 mg. or higher dilutions of tuberculin in persons who have received BCG should raise suspicion of a tuberculous infection with virulent organisms.

HARTENSTEIN, MILWAUKEE.

THE EUROPEAN BCG VACCINATION PROGRAM. R. PUNTIGAM, Wien. klin. Wchnschr. **61**:840 (Dec. 2) 1949.

In conjunction with the meeting in Copenhagen in the fall of 1949 the European BCG vaccination program is discussed. Some controversial points of tuberculin tests are discussed shortly, as well as the preparation and desirable standardization of tuberculin. Some remarks are made concerning investigation and statistics. The most recent figures of mass vaccination in Europe are given as 10,685,103 tuberculin tests with 5,579,248 vaccinations.

AMBERG, Rochester, Minn.

DEVELOPMENT AND PERSISTENCE OF TUBERCULIN REACTION AFTER BCG. I. BLUHM, Nord. med. **39**:1673 (Sept. 17) 1948.

Studies on 400 cases mostly of children are presented. The vast majority of the reactions became positive within six to eight weeks after vaccination, but sometimes it could take three to six months. Of 74 vaccinated persons living in tuberculous enviromnents, all remained tuberculin-positive up to 10 years after vaccination, while 61 persons out of 326 vaccinated (15.3%) living in tuberculous-free surrounding had become tuberculin-negative within the same period.

WALLGREN, Stockholm, Sweden.

TUBERCULIN TEST BY ORDINARY PIRQUET, ADRENALIN-PIRQUET AND MANTOUX. O. M. ANDENAES, Nord. med. **39**:1676 (Sept. 17) 1948.

Old tuberculin from the State Veterinary Institute in Oslo was used for the Pirquet test and old tuberculin from the State Serum Institute in Copenhagen with added epinephrine was used for the epinephrine Pirquet test. With the former method only 3.6% of the persons with positive reactions to 1 mg. in the Mantoux test gave negative reactions among the examined 611 persons aged 15 to 30 years. None gave a negative reaction to the epinephrine Pirquet test. The author concludes that this test is nearly as sensitive as the 1 mg. Mantoux test.

WALLGREN, Stockholm, Sweden.

DURATION OF IMMUNITY AFTER BCG VACCINATION. HERBERT ENELL, Svenska läk.-tidning. **49**:1225 (May) 1952.

Voluntary BCG vaccination was introduced in the public schools of Stockholm in 1945. Seventy-nine per cent of 4,000 children were vaccinated in 1951; only 3 of them were tuberculin negative at the follow-up study. About 90% of the vaccinated children were still tuberculin positive seven to eight years after vaccination. Of the unvaccinated tuberculin-negative school children 5.1% had acquired a clinical tuberculous disease after they started school. The corresponding figure for the vaccinated children is 0.16%.

WALLGREN, Stockholm, Sweden.

STUDIES WITH RADIOACTIVE BCG VACCINE. L. STRÖM and G. WIDSTRÖM, Svenska läk.-tidning. **49**:1285 (May) 1952.

The difference in reaction between tuberculin-positive and tuberculin-negative persons was studied by means of marked BCG vaccine. In the tuberculin-negative persons the marked BCG bacilli were transported very rapidly to the regional glands, while in the tuberculin-positive persons they remained much longer at the site of injection and were transported very slowly to the glands. In persons vaccinated with BCG, without any acquired tuberculin sensitivity, the marked BCG bacilli behaved as in tuberculin-positive vaccinated persons.

WALLGREN, Stockholm, Sweden.

DIAGNOSTIC BCG REACTION. HANS JACOB USTVEDT and ANTON AANONSEN, Tidsskr. norske lægefor. **68**:69 (Feb. 15) 1948.

A diagnostic BCG test is described. Two scratches are made through a drop of fluid of a strength of 20 mg. of BCG per milliliter. The reaction is read after six days. A papule formation is considered a sign of active tuberculous infection. The authors maintain that this test is more sensitive and more specific in tuberculous infection than are Mantoux tests.

WALLGREN, Stockholm, Sweden.

TREATMENT OF CONGENITAL SYPHILIS WITH PENICILLIN. A. M. J. DRESSELHUYS, Maandschr. kindergeneesk. **20**:333 (Nov.) 1952.

In the Children's Hospital in the Hague *32* children with congenital syphilis were treated from 1946-1950 with a single course of penicillin. The total amount of penicillin, divided into three hourly doses during 15 days, was at least 1,000,000 units. Three children died during, or shortly after, treatment. In one boy of 4½ years a negative Wassermann reaction developed but the Kahn and Meinicke reactions remained positive. The remaining *27* children, all under 1½ years, became seronegative within six months after treatment, and none of these have shown any clinical or serological relapses so far.

FROM THE AUTHOR'S SUMMARY.

Diseases of Blood, Heart and Blood Vessels, and Spleen

CEREBRAL CIRCULATION AND METABOLISM IN SICKLE CELL AND OTHER CHRONIC ANEMIAS, WITH OBSERVATIONS ON THE EFFECTS OF OXYGEN INHALATION. A. HEYMAN, J. L. PATTERSON, and T. W. DUKE, J. Clin. Invest. **31**:824 (Sept.) 1952.

Sickle cell anemia may be associated with a variety of serious cerebral manifestations. These symptoms are usually attributed to thromboses of the cerebral vessels produced by sickled erythrocytes, vascular stasis, and degenerative changes in the smaller arteries of the central nervous system. In chronic anemias from various causes mental manifestations are often seen. A diminution in cerebral oxygen consumption in patients with pernicious anemia has been reported and may be the basis for the alterations in the mental status seen in these patients.

For these reasons, the authors studied the cerebral circulation and metabolism in a group of patients. The cerebral blood flow, cerebral oxygen consumption, and cerebral vascular resistance were determined by the nitrous oxide technique, before and during the administration of 85 to 100% oxygen, in 10 patients with sickle cell anemia and in 8 patients with chronic anemia of other types, none of whom showed mental symptoms or neurologic involvement.

The mean cerebral blood flow for the patients with anemia as a group was significantly elevated, while the mean cerebral oxygen consumption was moderately reduced below that for control subjects. There were only small differences between the mean values for cerebral blood flow and cerebral oxygen consumption in the two groups of anemic patients.

The administration of 85 to 100% oxygen to the patients with anemia was generally followed by a decrease in the cerebral blood flow and an increase in cerebral vascular resistance comparable to the values found for the control subjects. The cerebral oxygen consumption in many of the patients with anemia showed a rise during oxygen inhalation.

Heyman and his colleagues believe that the increase in cerebral blood flow in chronic anemia is caused by the combined effect of reduction in blood viscosity and vasodilatation from reduction

in arterial, mean capillary, and venous oxygen tensions. They further suggest that the reduction in cerebral metabolism, and possibly to some extent the mental symptoms, observed in chronic anemia may be due to chronic tissue hypoxia. The use of oxygen may therefore be a rational emergency therapeutic measure in such cases when mental symptoms are present.

ALPERS, Philadelphia [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

METABOLIC STUDIES IN PERNICIOUS ANEMIA: NITROGEN AND PHOSPHORUS METABOLISM DURING VITAMIN B_{12}-INDUCED REMISSION. G. WATSON JAMES III and LYNN D. ABBOT JR., Metabolism **1**:259 (May) 1952.

During the remission induced by administration of vitamin B_{12}, positive nitrogen balance was found to exist and there was evidence of synthesis of blood proteins from nondietary sources. Patterns of excretion of phosphorus and uric acid suggested that vitamin B_{12} exerted a direct influence on nucleoprotein metabolism during the change from a megaloblastic to an erythronormoblastic marrow.

KAPLAN, Cincinnati.

ACTH AND SPLENECTOMY IN IDIOPATHIC ACQUIRED HEMOLYTIC ANAEMIA. N. FELDMAN and H. C. FALCKE, South African M. J. **26**:778 (Sept. 27) 1952.

A child with hemolytic anemia was treated with transfusion until she became refractory; corticotropin (ACTH) therapy failed to give lasting results, and splenectomy was done, with rapid and dramatic improvement.

MCGUIGAN, Evanston, Ill.

APLASTIC ANEMIA (CHRONIC ERYTHROBLASTIC PHTHISIS) AND CORTISONE. C. GASSER, Schweiz. med. Wchnschr. **50**:1241 (Dec. 15) 1951.

A prematurely born girl of 2,500 gm. birthweight developed normally until at 10 months of age she had uncomplicated measles. Since then increasing pallor, fatigue, and irritability were noted. At an age of 14 months the number of erythrocyes was 1,300,000. The hemoglobin was 25%. No other striking abnormalities of the circulating blood were found except a very high sedimentation rate. In the bone marrow 5% erythroblasts were counted. In spite of treatment, the erythroblasts disappeared entirely from the bone marrow. Four months after admission to the hospital, cortisone was given in a dosage of 10 mg. daily without definite improvement. After a lapse of about 3 months cortisone therapy was resumed, but the dosage was increased to 75 mg. daily. The erythroblasts increased strikingly in the bone marrow, but transfusions were necessary to overcome the anemia. When cortisone medication was gradually suspended, the bone marrow again became depleted of erythrobasts, but when treatment was resumed the same good results were obtained. It seems that the erythroblasts produced during corisone therapy need a special factor to become mature. At the time of the report, about three months after use of the larger dose of cortisone was begun, the drug could be reduced to a small daily dosage without transfusions.

AMBERG, Rochester, Minn.

INVESTIGATIONS OF THE "CONSTITUTIONAL THROMBOPATHY (V. WILLEBRAND-JUERGENS)" IN THE ISLES OF ÅLAND. R. JÜRGENS and H. FORSIUS, Schweiz. med. Wchnschr. **50**:1248 (Dec. 15) 1951.

Among 200 members of five families, 26 bleeders were registered. Bleeding occurred into skin, mucous membranes, muscles, genitals, joints, retina, and conjunctiva. The bleeding time was increased, and an increased fragility of the capillaries was demonstrable. The number of thrombocytes and megakaryocytes was normal, but morphological abnormalities were seen. For illustration the findings in eight patients are tabulated; the list includes two boys, one 11 and the other 13 years of age. In some a deficient prothrombin consumption was registered. A slowing of thrombus formation and a slightly increased coagulation time, as well as a marked diminution of the elasticity of the thrombus, could be elicited. The hemorrhages in cases of constitutional thrombopathy are due to decreased agglutinability of the thrombocytes and disturbance of the first phase of coagulation, that is, activation or formation of thrombokinase. Furthermore, a vascular disorder exists. The 11-year-old boy had a very severe epistaxis which could be stopped immediately on application of a thrombin preparation.

AMBERG, Rochester, Minn.

THE ACTION OF VITAMIN B_{12} ON THE PRODUCTION OF ERYTHROCYTES IN VITRO. P. PERITI and G. FOWST, Riv. clin. pediat. **49**:654 (Sept.) 1951.

The action of vitamin B_{12} on red blood cells from rabbit bone marrow has been investigated in vitro with use of a modification of Magnussen's technique.

Vitamin B_{12} appeared to be essential for the survival of the cells. Concentrations between 0.4 and 0.8 γ per milliliter stimulated erythrocyte formation, whereas higher concentrations had a remarkable inhibiting effect, the intensity of which appeared related to the dose, reaching a maximum at levels of 1 to 1.5 γ per milliliter.

FROM THE AUTHOR'S SUMMARY.

BONE MARROW APLASIA TREATED WITH CHLOROMYCETIN. LUIS MARENO SOUMASTRE, Rev. chilena pediat. **23**:393 (Sept.) 1952.

The authors report a case of an 8-month-old infant, who presents a picture of aplasia of the bone marrow which started two weeks after receiving two courses of chloramphenicol in doses of 112 mg. per kilogram of weight during 12 days. The changes in the bone marrow continued in a progressive manner and produced the death of the child four months after the first hemorrhagic manifestations appeared. The absence of other etiological factors and the close relationship existent between the ingestion of the chloramphenicol and the appearance of the blood picture allows them to attribute this to a toxic action of the antibiotic on the bone marrow of the patient.

FROM THE AUTHOR'S SUMMARY.

PROBLEMS OF LEUKEMIA IN CHILDREN. K. WEISSE, Ztschr. Kinderh. **67**:582, 1950.

The author observed that the number of cases of leukemia in children has increased during the last 25 years, that more subacute cases and aleukemic forms have occurred, and that joint pains have become more frequent.

GLASER, JERUSALEM.

ACUTE AND CHRONIC LEUKEMIAS IN CHILDHOOD AND ADOLESCENCE. P. MAURICE, Acta paediat. belg. **6**:5, 1952.

From one case report and the study of 25 cases of acute and chronic leukemia observed at the Saint-Pierre Hospital between 1940 and 1950, the author discusses the problem of treatment. He comes to the conclusion that roentgen therapy and radioactive phosphorus act best in cases of chronic leukemia, urethan acts best in chronic myeloid leukemia, folic acid antagonists act best in acute lymphatic leukemia, and nitrogen mustard in Hodgkin's disease. Blood transfusions and especially exsanguination transfusions are the therapy of choice. Corticotropin and cortisone can produce remissions in acute and chronic cases but the effect seems to be of short duration.

GLASER, Jerusalem.

THE CLINICAL ASPECT OF CONGENITAL HEMOLYTIC JAUNDICE IN CHILDREN. OTTO HRODEK, Pediat. listy **7**:279, 1952.

The clinical features and laboratory findings in congenital hemolytic jaundice in childhood are discussed and evaluated on the basis of personal experience with 19 children up to 13 years of age, of whom 10 underwent splenectomy. In almost half of the cases it was possible to trace back the first manifestations of the disease into very early childhood, in 9 of them as far back as 6 months, in the remaining 10 back to 6 years. Those with splenectomy were examined for the first time on an average of one and one-half years after the first manifestations, those conservatively treated after three and one-half years. Splenectomy was performed on an average of one and one-fourth years after the first examination at an average age of 6 years (in one at 7 months, in another at 15 months). Anemia in early childhood was always prominent, while jaundice remained a less conspicuous feature. Splenomegaly is the rule; hepatic enlargement is less extensive and less common. Twice hematogenous jaundice was combined with jaundice of hepatic origin. Complications of liver and bile ducts are not as common in the child as in the adult. The frequency of crises with violent abdominal pain, resembling sometimes an acute abdominal disease is also greater at a later age.

A case of an acute crisis is described, in which there was marked pancytopenia and an obvious inhibition of maturation in the red marrow. This may be explained in accordance with the views of Dameshek and Heilmeyer and through the mechanism of depressive and hemolytic hypersplenia. Stress is laid on the necessity early splenectomy to prevent development and growth retardation.

FROM THE AUTHOR'S SUMMARY.

MONONUCLEOSIS AND PSEUDOMONONUCLEOSIS. B. VAHLQUIST, Svenska läk.-tidning. **49**:3153 (Dec.) 1952.

Multiple cases of a disease in children similar to infectious mononucleosis were observed. The clinical symptoms consisted of rhinopharyngitis or gastrointestinal disorders and sometimes micropolyadenia, slight splenohepatomegalia, and rheumatic pains. None of the patients showed diphtheroid tonsillitis or marked glandular enlargement. The sedimentation rate was moderately increased. In no case was the Paul-Bunnel reaction positive. The abnormal blood picture persisted for a long time, several months to one year or more. Sometimes there was a slight increase in the total white cell count; the blood picture was characterized by cells similar to McKinley cells, up to 50% or more, and in addition monocytic and lymphocytic transition cells were present. The same blood picture was found also in older children and adults. The polymorphonuclear cells were normal.

WALLGREN, Stockholm, Sweden.

EFFECT OF INTRAVENOUS INJECTIONS OF SUSPENSION OF BLOOD PLATELETS: CERTAIN CONDITIONS CHARACTERIZED BY THROMBOPENIA AND THROMBOPATHY. S. VAN CREVELD, M. M. P. PAULSSEN, and H. L. J. M. BARTELS, Maandschr. kindergeneesk. **20**:249 (Sept.) 1952.

The authors report on the preliminary results obtained in a number of children with primary and secondary thrombocytopenia and in two children with thrombopathy, in which intravenous injections of suspensions of platelets were given. The technique for the isolation of platelets from human blood is described. The action of these injections on the platelet count, the clotting time, and the clot-retraction is studied; also the duration of the action is recorded. Usually this action was observed during 2 to 4 days (after injection of the platelets). The value of these injections for the prevention and treatment of hemorrhages associated with thrombocytopenia and thrombopathy is stressed. In some cases of thrombocytopenia the increase in platelet count reached normal values, which persisted or lasted several weeks.

FROM THE AUTHORS' SUMMARY.

ACQUIRED HEMOLYTIC ANEMIA: EXTENDED OBSERVATIONS OF A PATIENT TREATED WITH CORTICOTROPIN AND CORTISONE. J. I. DE BRUIJNE and S. VAN CREVELD, Maandschr. kindergeneesk. **20**:321 (Nov.) 1952.

A 4-year-old girl, suffering from severe acute acquired hemolytic anaemia of unknown origin was treated with ACTH (corticotropin), after it had become apparent that blood transfusions did not improve the hemolytic process. Several courses of treatment were given, but they had no lasting effect. After splenectomy a very severe hemolytic crisis followed. By means of a maintenance dose of cortisone first given intramuscularly, later orally, the patient is in good condition and has remained so for 10 months.

FROM THE AUTHORS' SUMMARY.

Diseases of Nose, Throat, and Ear

RHINITIS MEDICAMENTOSA. JAMES S. WALKER, J. Allergy **23**:183 (March) 1952.

A group of five adults is reported in which either privine or phenylephrine (Neo-Synephrine) or both had been used over a long period of time for the relief of nasal obstruction without permanent relief. Symptoms were relieved with cessation of the use of the drugs. The author believes that rhinitis from medication occurs more often than suspected. A diagnosis can be made by a good history, and the absence of other causative factors such as infection, allergy, or mechanical obstruction. Relief is accomplished by the withdrawal of the offending agent.

HOYER, Cincinnati.

STUDY OF WORD APPROXIMATIONS IN THE SPONTANEOUS SPEECH OF INFANTS. WILLIAM H. MCCURRY and ORVIS C. IRWIN, J. Speech & Hearing Disorders **18**:133 (June) 1953.

It is possible to get observer agreement as to the meaning of vocalizations for infants at the 10th and the 11th age level (20 to 22 months). There is a significant increase in the number of word approximations from the 10th to the 11th age level and a significant increase in the number of words attempted. There was no increase in the number of correct pronunciations from one age level to another. There were no sex differences which were significant.

PALMER, Wichita, Kan.

NORMS FOR MAXIMAL REPETITIVE RATES FOR CERTAIN SOUNDS ESTABLISHED WITH THE SYLRATER. John V. IRWIN and ORVILLE BECKLAND, J. Speech & Hearing Disorders **18**:149 (June) 1953.

A new instrument, the Sylrater, which does not require direct connection with the subject, is described, and tentative norms of repetitive rates of speech and nonspeech sounds are established for ages 6, 7, 9, 11, 13, and 15 years both for boys and girls. The range of rates is quite wide. The general level of the correlation fails to indicate that any single measure such as a repeated sound may be safely taken as an accurate index of the ability to execute rapid, repetitive movements.

PALMER, Wichita, Kan.

INVESTIGATION OF THE DEFINITION AND USE OF THE DIAGNOSIS "PRIMARY STUTTERING." PHILIP J. GLASNER and FRANA DAHL VERMILYEA, J. Speech & Hearing Disorders **18**:161 (June) 1953.

One hundred seventy-one members of the American Speech and Hearing Association replied to a questionnaire on the definition of primary stuttering. There is a general lack of agreement among these persons as to what constitutes this condition.

PALMER, Wichita, Kan.

SOME INDIANS WHO STUTTER. EDWIN M. LEMERT, J. Speech & Hearing Disorders **18**:168 (June) 1953.

Field contacts, interviews, and observations covering eight reserves of Salish Indians, Kwakiutl, and one Nootka, located on the coastal mainland of British Columbia and Vancouver Island, showed that these Indians do stutter. Two cases were reported specifically. Some stutterers in this study had been children between 1865 and 1880, an age which precedes or barely coincides with the establishment of the first religious missions in the area. The author believes that the culture of these Indian tribes is not the same as that of the Bannock and Shoshone tribes reported by Johnson, Snidecor, and Bullen in which stuttering is reported not to have been present.

PALMER, Wichita, Kan.

SPHYGMOAUDIOMETRY: THE NEW METHOD TO TEST OBJECTIVE HEARING. A. VASSALLO DE MUMBERT, Bol. españ. otorrhinolaring. y bronchoesofagol. **5**:37, 1952.

De Mumbert describes a new technique for testing objective hearing. This technique which he has developed accidentally occurred to him while examining a patient. He coordinates the radial pulse pressure with the various frequencies of the tonal scale and notes the definite changes in the pulse pressure with the increase in intensities at the various frequency levels. This is based on the fact that the acoustic and the vestibular triangular nuclei situated in the floor of the fourth ventricle have an intimate relationship through a somaticovegetative anastomosis with the nucleus of the vagus nerve. Hence, the stimulus to the acoustic nuclei would cause a marked vasodepressor action on the circulatory system, thus causing a momentary fall in arterial pressure. After making these observations de Mumbert constructed a suitable apparatus for recording automatically on a dial the blood pressure reading and the influences on the curve by variations in the intensity at the definite frequencies. This method of examination is extremely important because it can be used in testing very small children, even infants; older children

who do not cooperate properly with other procedures; adults whose objective responses are obtained without any voluntary influence on the part of the patients; deaf-mutes; mentally rearded patients; patients with psychogenic disturbances, and those patients presenting medico-legal complications. This method is well worth investigating.

PERSKY, Philadelphia [A. M. A. ARCH. OTOLARYNG.].

Diseases of Lungs, Pleura, and Mediastinum

CYSTIC HYGROMA OF THE NECK AND MEDIASTINUM SUCCESSFULLY TREATED BY ROENTGEN RAYS. GEORGE E. PFAHLER and HENRY H. PERLMAN, Am. J. Roentgenol. **63**:539 (April) 1950.

Pfahler and Perlman believe that roentgen therapy should be given first consideration in the treatment of cystic hygroma. The amount of radiation estimated to be necessary would not interfere with any operative procedures if subsequent surgery seems advisable. Operation should not be considered if the mediastinum is involved. The authors feel that x-rays are more appropriate than radium.

HARRISON, Oak Park, Ill.

DENTOBRONCHITIS. G. M. H. VEENEKLAAS, Ann. paediat. **178**:59 (Jan.) 1952.

Three patients suffering from chronic bronchitis are described. They also had considerable dental caries. There were no other pathological findings which might have caused bronchitis. The treatment of the caries, carried out two years or longer thereafter, was followed by disappearance of the bronchitis.

In three other patients symptoms of bronchitis were not found after treatment of the caries. On acount of the brief time of the observation (one year) they are not described. In the absence of other oral pathology, aspiration of material from the carious elements is considered to be the cause of the bronchitis.

FROM THE AUTHOR'S SUMMARY.

THE ERRONEOUS PLACEMENT OF CHILDREN WITH BRONCHIAL DILATATIONS IN SANATORIAL CARE. V. CHEVALIER, Acta pediat. belg. **6**:111, 1952.

From a consideration of various examples and roentgenograms the author discusses cases of old fibrosed and/or calcified pulmonary lesions of tuberculous children and children with bronchiectasis who were placed in sanatorial care. He emphasizes the psychological damage done to these children and insists on the need for thorough examination and prolonged observation before a child is placed in a sanatorium.

GLASER, Jerusalem.

CONTRIBUTION TO THE VIRUS ETIOLOGY OF INTERSTITIAL PLASMA CELL PNEUMONIA IN EARLY INFANCY. C. HALLAUER, Schweiz. med. Wchnschr. **82**:409 (April 12) 1952.

During a period 1946-1951, pieces of the lungs of 12 young infants were obtained. The cause of death was interstitial plasma cell pneumonia of early infancy. Transmission of virus was tried in various animals as well as on chick embryos. It seems at least possible that persistent passage of the pneumonia-producing agent may be obtained on chick embryos. Results of tests with human and animal immune and normal sera were not absolutely convincing. However, the serum of two mothers of infants which had succumbed to the disease possessed (compared with controls) a definite and probably significant protective activity. It is concluded that the virus etiology of the interstitial plasma cell pneumonia of early infancy has not been established securely.

AMBERG, Rochester, Minn.

Diseases of Gastrointestinal Tract, Liver, and Peritoneum

RECURRENT SMALL INTESTINAL INTUSSUSCEPTION IN CHILDREN. M. D. TEITELBAUM and NATHAN ARENSON, Am. J. Roentgenol. **63**:80 (Jan.) 1950.

Five cases of intussusception occurring in the small intestine of children are presented. Roentgenograms of four cases are reproduced. In three cases the intussusceptions were multiple, and in two cases they were recurrent.

HARRISON, Oak Park, Ill.

UTILIZATION OF CHOLANGIOGRAM DURING EXPLORATION FOR BILIARY ATRESIA. ORVAR SWENSON and JOHN H. FISHER, New England J. Med. **247**:249 (Aug. 14) 1952.

The authors present a method by which patency of the biliary system in infants with increasing obstructive jaundice may be demonstrated by the instillation of radiopaque dye into the gall bladder. There are two advantages in this method: (1) the small surgical procedure involves a minimal risk to the patient, and (2) there is no chance of traumatizing the small ducts with this diagnostic method. It is postulated that some of the cases, diagnosed as cases of biliary atresia because of the examiner's inability to demonstrate a patent extrahepatic biliary tree, fall into the group of mucoviscidosis.

WHEELOCK, Denver.

FACIAL SKELETON MEASUREMENTS AND TONGUE CARRIAGE IN SUBJECTS WITH REPAIRED CLEFT PALATES. MCKENZIE BUCK, J. Speech & Hearing Disorders **18**:121 (June) 1953.

Twenty patients with repaired unilateral cleft of the velum and lip with I. Q. above 70 and a hearing loss of not more than 20 db. were compared to 20 normal speakers on the basis of chronological age and sex. Vertical and anteroposterior dimensions of the face are smaller for the cleft-palate group. Midsagittal tongue measurements are smaller for the cleft-palate group, and the tongue is held lower in the mouth. Insufficient mouth opening is probably not related to nasality in the person with cleft-palate.

PALMER, Wichita, Kan.

ABILITY OF INFANTS TO TASTE PTC: ITS APPLICATION IN CASES OF DOUBTFUL PATERNITY. HUGO M. CARDULLO and L. EMMETT HOLT JR., Proc. Soc. Exper. Biol. & Med. **76**:589 (March) 1951.

Phenylthiocarbamide (PTC) has been found to be tasteless to some persons but extremely bitter to others. The characteristic taste seems to be limited to the C = S linkage. In the study of 203 families about two-thirds were considered as tasters and one-third nontasters, the ability to taste being inherited as a dominant characteristic and the inability to taste as a recessive trait. Study was undertaken to determine whether the ability to taste PTC might be applied in cases of doubtful paternity. The ability to taste was graded on a 1 + to 4 + basis, 1 + indicating merely salivation or a few "mouthing" movements and 2 + to 4 + grimacing, crying, and even retching. It was a surprise to the authors how readily the ability to taste this material could be detected even in premature infants. The accompanying illustrations are excellent. The authors used a 1:10,000 dilution and studied the effect in 93 babies (18 prematures, 37 full-term, and 38 1 week to 2 years of age). In this study 57 infants (61.3%) were tasters and 36 (38.7%) nontasters. Age and sex did not appear to affect the distribution. The authors believe that data such as these can be profitably employed in cases of doubtful paternity when a tasting child is born to a nontasting mother. The authors point out that the medicolegal application has received attention in France, as indicated by the exhibit at the Sixth International Pediatric Congress in Zurich by Lamy, Pognan, Schweissguth and Fauvert.

HANSEN, Galveston, Texas.

CONGENITAL DIAPHRAGMATIC HERNIA. J. H. EBBS and H. H. MCGARRY, Canad. M. A. J. **67**:115 (Aug.) 1952.

Points in the diagnosis of diaphragmatic hernia are discussed, and it is shown that earlier diagnosis and earlier repair give a much better prognosis. In early infancy the cyanosis may be confused with congenital heart disease, intracranial hemorrhage, atelectasis, or tracheoesophageal fistula. In later childhood signs and symptoms depend largely on the varying amounts of intestine and intestinal content present in the chest cavity. No mention is made of the scaphoid abdomen in newborn infants as a diagostic point.

MCGUIGAN, Evanston, Ill.

A Case of Fibrocystic Disease of the Pancreas with Intestinal Obstruction. Emmanuel Levy, Arch. Dis. Childhood **26**:338 (Aug.) 1951.

A case of fibrocystic disease of the pancreas is described. The patient died from intestinal obstruction at the age of 7 months. The relation between meconium ileus and the celiac phase of this disease is discussed. Attention is drawn to the possibility of overlooking fibrocystic disease of the pancreas as a cause of intestinal obstruction after the first few days of life. The literature on fibrocystic disease of the pancreas with intestinal obstruction is reviewed.

Kelly, Milwaukee.

Pathological Embryology of the Esophageal-Tracheal Anlage and the Embryogenesis of a Congenital Esophageal-Tracheal Communication. W. Galluzzi, Lattante **24**:137 (March) 1953.

The various theories as to the cause of congenital atresia of the esophagus, with or without a tracheal-esophageal fistula, are listed and discussed. Most of these theories explain satisfactorily only the commonest of the several types of esophageal atresia. The author presents his own hypothesis, whereby he is able to explain the origin of all the types. He suggests that there has been an incomplete formation of the mesodermal coat of that part of the foregut containing the tracheoesophageal anlage; this leads to the defect when the otherwise normal embryological development of the anlage has occurred.

Higgins, Boston.

Carrot Flour in the Treatment of Dyspepsia and Enteritis in Infants. G. Bulla, Lattante **24**:175 (March) 1953.

An Italian preparation of carrot flour (Elonac) was used with excellent clinical results in the treatment of 60 infants with dyspepsia and/or diarrhea of various degrees of severity. One hundred fifty to 200 cc. per kilogram of body weight of a 7% concentration of the flour in water was the only food given for the first days of the illness.

Higgins, Boston.

Congenital Mesenteric Adhesions with Stenosis of the Second Part of the Duodenum. Angel Crespo Santillana, Acta pediat. españ. **7**:1543 (Dec.) 1949.

Dr. Santillana reports the case of an infant with a history of projectile vomiting, asphyxia, and prematurity. The child's weight at birth was 2,000 gm. The family history complicated the diagnosis because it suggested both tuberculosis and syphilis.

The mother had several abortions, carrying each pregnancy a little longer; the infant in this case was born alive, although premature. However, blood Wassermann tests were negative for mother, child, and father.

The mother had pleurisy in her early life before her marriage, and the father suffered from atypical asthma. All tests for tuberculosis, however, were also negative.

The use of atropine had proved ineffective, and, since no mass could be palpated, the usual pyloric stenosis was ruled out. The possibility of intracranial hemorrhage was also ruled out.

The vomiting was irregular, sometimes immediately after nursing, sometimes following a harsh cough, and frequently there was violent straining with the vomiting. The peristaltic waves were unusually hyperactive, but not of the kind associated with pyloric stenosis.

The child gained very slowly and had one bout of pneumonia, which was treated with penicillin with satisfactory results. Needless to say, all types of feedings, including vitamin therapy and parenteral injections, were tried.

A blood cell count ruled out the possibility of a blood dyscrasia.

After the pneumonia, the "coffee ground" type of vomiting did not disappear, and finally permission was given for roentgenological study and possible surgery. The author gives a very detailed and masterful discussion of the causes of vomiting in the newborn and his reasons for ruling out practically all of these before the x-ray studies were made.

With a nasal Nélaton catheter No. 15 barium was injected; there were dilatation of the esophagus and esophageal varices and great dilatation of the stomach. However, barium passed into the stomach and pylorus and into the first portion of the duodenum in a normal manner. X-rays are included.

An operation was done when the girl was 8 months; obstruction was found at the union of the first and second portions of the duodenum. There were smaller adhesions and malrotation of the mesentery.

These were relieved and the stenosis of the second portion treated in a way similar to that usually employed for pyloric stenosis.

In postoperative therapy, plasma solutions of the proper electrolytes and oxygen were used. Human milk was given for feeding. Metrazol (pentomethylenetetrazol) was necessary at one time, and phenobarbital for sedation occasionally was necessary. Pathological studies gave no evidence of tuberculosis, and a congenital anomaly was decided to be the cause.

A month after the operation, x-ray studies showed the stomach, duodenum, etc., to be normal, and the child was growing and gaining weight.

After two years the little girl is growing normally, slightly retarded but having a normal dentition and psychic development.

ALLEN, San Francisco.

TREATMENT OF MEGALCOLON IN THE CHILD. GUILLERMO ZIEGLER and LUIS FUENTES DE LA, Rev. chilena pediat. **23**:376 (Sept.) 1952.

Swenson's operation modified by Hiatt is recommended as the only rational treatment for congenital megacolon. On the other hand, for idiopathic megacolon medical treatment should be tried before thinking of a surgical intervention, which can be the same Swenson's operation or a simple resection of the dilated portion of the sigmoid flexure depending on the case. These operations can be performed at any age.

FROM THE AUTHORS' SUMMARY.

THE ACTION OF STREPTOMYCIN IN TOXICOSIS AND DYSPEPSIA. A. LOESCHKE and A. COCHLOVIUS, Arch. f. Kinderh. **136**:154, 1949.

The authors report observations on 13 infants, 2 weeks to 7 months old, with severe dyspepsia and toxicosis who were treated with streptomycin given orally by bottle or by tube feeding in doses of 25 to 75 mg. half an hour before feedings, five to eight times in 24 hours. No other dietetic measures were used. There were four deaths in this series, but in the remaining nine infants remarkable improvement was seen within 24 hours after the start of streptomycin therapy. Bacteriologic examinations revealed diminution, even complete disappearance, of Escherichia coli from the feces after the oral administration of streptomycin.

ARON, Chicago.

RADIOGRAPHIC OBSERVATIONS OF THE DIAPHRAGM IN CHILDREN. W. SWOBODA, H. BITTNER, and VAN DER HECHT, Acta paediat. belg. **6**:117, 1952.

The authors observed an anomaly of the diaphragm and the liver which presents itself in the anteroposterior roentgenogram as a bulge of the medial portion of the right diaphragm and in the lateral view as an anterior bulge. In three cases coming to autopsy for other reasons the authors found a bulge in the liver with normal liver parenchyma and a thinning of the diaphragm, with complete absence of muscle fibers over this area. They consider this a congenital malformation and believe that this anomaly occurs in constitutionally weak children.

In differential diagnosis they consider mediastinal or interlobal pleurisy, pulmonary infiltration, tumors of lungs or mediastinum, esophageal diverticulum, tumors, cysts, or abscess of the liver or subdiaphragmatic space, and diaphragmatic hernia.

GLASER, Jerusalem.

OUR EXPERIENCE WITH ANTIBIOTICS IN THE TREATMENT OF DIARRHEA IN CHILDREN. L. PELIKAN, Pediat. listy **5**:281, 1951.

The etiology of diarrhea in children and present methods of treatment are briefly described. The results of treatment with chemotherapeutic drugs, penicillin, streptomycin, aureomycin, and chloramphenicol (Chloromycetin) are evaluated from the statistical material. It was found that in the treatment of the toxemias, chloramphenicol gave the best results; aureomycin only slightly less good; streptomycin was of little value; and chemotherapy was unsuccessful.

FROM THE AUTHOR'S SUMMARY.

INTERMITTENT INTESTINAL OCCLUSIONS CAUSING INCOMPLETE ROTATION. V. TOSOVSKY, Pediat. listy **6**:45, 1951.

Description is given of the so-called Ladd syndrome as the basis of malrotation, in a girl of 2 years, successfully treated by Ladd's transposition operation.

FROM THE AUTHOR'S SUMMARY.

THE THERAPEUTIC USE OF ANTIBIOTICS IN THE TREATMENT OF INFANTILE DIARRHEA BY ESTABLISHING THE COMPLEX SENSITIVITY OF THE INTESTINAL FLORA. M. DVORACEK, A. KUBOVY, and J. DVORAK, Pediat. listy **7**:291, 1952.

Stools from 267 children were examined for the complex sensivitiy of the intestinal flora to antibiotics, according to the method described. In vitro, chloramphenicol was the most sensitive, streptomycin next, and then aureomycin. The best clinical response was to chloramphenicol, then to aureomycin and lastly to streptomycin. The described method of testing the complex sensitivity of the flora in cultures, prepared directly from the enteric stools of children, approximates most closely to conditions in vivo. The complex sensitivity method determines most rapidly the most effective antibiotic in the treatment of infantile diarrhorea.

FROM THE AUTHORS' SUMMARY.

OBSERVATIONS ON THE CEREBROSPINAL FLUID IN INFANTILE DIARRHEA. NIILO HALLMAN and HILKKA TAHKA, Acta pædiat. **41**:337 (Sept.) 1952.

A study of the cells in the spinal fluid, as well as the Nonne and Pandy reactions, was made in 211 cases of infantile diarrhea of various degrees of severity.

The number of cells in the cerebrospinal fluid was invariably (two to four examinations) below 5 per cu. mm. in 100 cases, and it was found to be increased at least once as follows: 6 to 10 per cu. mm. in 30 cases, 11 to 20 per cu. mm. in 35, 21 to 50 per cu. mm. in 29, 51 to 100 per cu. mm. in 7, and over 100 per cu. mm. in 11 cases. The changes are generally more extensive in the severe cases, but the difference between them and the mildest cases, in which no symptoms pertaining to the central nervous system were exhibited, was not particularly significant. The majority of the cells were identified as lymphocytes.

If the protein reactions are also taken into consideration, the spinal fluid was found to be within normal limits in only 13 patients.

The age at onset, the weight of the infant as compared with the expected weight, the alkali reserve on admission and other simultaneous infections do not seem to have any noteworthy effect on changes in the spinal fluid.

Changes were found to be more frequent in diarrhea produced by the Shigella (35 cases) than in cases due to an unknown causative agent.

Bacterial staining and culture of the cerebrospinal fluid were negative in all cases.

FROM THE AUTHORS' SUMMARY.

OBSTIPATION IN PEDIATRIC PRACTICE. BERTIL SÖDERLING, Svenska läk.-tidning. **46**:421 (Feb. 25) 1949.

Söderling stresses the common occurrence of obstipation in small children and its complications: anal fissures, increased sphincter tonus, and deterioration of the general state of health, with fatigue, lassitude, anorexia, rectal incontinence, vomiting, neurosis, etc. The treatment is thoroughly discussed, and the importance of satisfactory supervision of the behavior of small children as to their bowel habit is emphasized.

WALLGREN, Stockholm, Sweden.

BACTERIUM COLI NEAPOLITANUM (BCN) IN AN EPIDEMIC OF INFANTILE DIARRHEA IN AN INFANTS' HOME. GUNNAR LAURELL and E. LYCKE, Svenska läk.-tidning. **49**:560 (Feb.) 1952.

At a children's home 27 of the children fell ill during an epidemic of diarrhea with Escherichia coli neapolitana in the stools. Twenty-three of the children were between 1 and 2 years of age, three between 2 and 3 years and one over 3 years of age. Only 2 of the 10 children older than

1½ years fell ill, both of them having a very mild infection. The isolation facilities at the home were bad, and the isolation precautions taken were not sufficient to stop the epidemic. After the outbreak of the epidemic no child under 1½ years of age was admitted to the institution, and bacillary carriers were treated with sulfaguanidine. After a couple of months the epidemic ceased and no specimen of the stools contained the organism.

WALLGREN, Stockholm, Sweden.

VITAMIN K IN THE TREATMENT OF ACUTE HEPATITIS. HANS-OLOF MOSSBERG, Svenska läk.-tidning. **49**:1577 (July) 1952.

A study of 178 cases of acute hepatitis is reported. Even in severe hepatic damage the prothrombin-producing function of the liver is not impaired, and the decrease of the prothrombin value in the blood depends principally on a deficient absorption of vitamin K from the intestines. Oral vitamin K treatment is as effective in occlusion jaundice as in acute hepatitis, but the effect of the treatment on the prothrombin value is apparent only in cases of severe acute hepatitis. Vitamin K treatment does not have any influence on the course of the hepatitis.

WALLGREN, Stockholm, Sweden.

Nervous Diseases

CONGENITAL TUMORS OF THE SPINAL CORD IN INFANTS. HENRY G. SCHWARTZ, Ann. Surg. **136**:183 (July) 1952.

Congenital intraspinal tumors in children are rare. Four cases are reported. There were two cases of dermoids, one of teratoma, and one of lipoma. In all cases, there was an associated skin defect consisting of a sinus, tract, or dimple. In two cases, intraspinal infection resulted from communication by way of dermal sinuses. Although these tumors are cytologically dissimilar, the location, gross behavior, and superficial appearance suggest a close relationship and a common potential source of origin at sites of normal as well as of abnormal fusion of embryonic germ layers.

BANTIN, Omaha.

GUIDES TO OPTIMAL THERAPY IN BACTERIAL MENINGITIS. HATTIE E. ALEXANDER, J. A. M. A. **152**:662 (June 20) 1953.

Optimal therapy is based on early adequate treatment with a safe bactericidal agent with a high enough blood level to kill the first and second generation mutants which become more resistant. The author has found subdural fluid to be a frequent complication; a conservative policy seems to be as effective as an aggressive policy at this writing. At long last the author has recommended a reduction in intrathecal therapy but has not quite capitulated. Her optimal therapeutic regimen in most of the common forms of pyogenic meningitis should be in everyone's notebook.

KIMBALL, Evanston, Ill.

RECURRENT HEADACHES IN CHILDREN: A STUDY OF 100 CLINIC CASES. GEORGE R. KRUPP and ARNOLD P. FRIEDMAN, New York J. Med. **53**:43 (Jan. 1) 1953.

This is a report on 100 children observed at the Montefiore Hospital, of whom 75 had migraine and 17 had tension headaches. A diagnosis of migraine is made when the pain is unilateral and is thought to be due to vasoconstriction of the cerebral arteries, especially of the branches of the unilateral external carotid. This phase is followed by distention and increased amplitude of pulsation. Tension headaches are often accompanied by emotional conflicts—anger, worry, and frustration. They are bilateral, frontal, or occipital. Frequency and duration are variable, but the headache "may last for weeks." Before the cases were studied a history of the patient and of his parents was recorded, and a thorough physical examination, including investigation of neurologic factors, electroencephalography, studies of visual fields, and blood studies. Psychologic tests were given at times. It was found that most migraine headaches appeared before the patients were 4 years old, difference in sex was of no importance, and 85% of the patients observed suffered from headaches. Children showed prodromal signs of gastric, visual, and psychologic disturbances. Arguments with their parents sometimes produced

headaches in both parents and children! The child with a high I.Q. seemed to be more subject to head pains. Medical treatment was with acetylsalicylic acid or 1 mg. of ergotamine tartrate plus 100 mg. of caffeine (Cafergot). The maximum dose (four tablets) was given at intervals of a half-hour to one hour. Improvement sometimes was found upon psychiatric investigation; this fact tends to prove the psychosomatic element. Adults should learn to observe a child's moods and not to enter into conflicts at an inopportune time. The prognosis for children is generally poor, since most adults with migraine were sufferers from headaches in childhood (at least 35% of them).

I. W. Voorhees, New York [A. M. A. Arch. Otolaryng.].

Intracranial Tuberculomas. R. A. Gonzales, J. Neurosurg. **9**:555 (Nov.) 1952.

Before the advent of streptomycin, the surgical treatment of cerebral tuberculoma was discouraging because of the common occurrence of postoperative tuberculous meningitis. In this paper, the experiences encountered in 10 consecutive cases of verified intracranial tuberculomas are recorded. In all 10 cases an operation was carried out. Three patients died and seven survived. The seven survivors were followed from 12 to 36 months, and all were living and well at the time of this report.

The author reviews the incidence, symptoms, and operative findings in this series and draws the following conclusions: Tuberculoma is a common intracranial lesion. It is more prevalent in the first two decades of life. The duration of symptoms may be from 2 to 35 months. A history of fever at the onset of symptoms may be obtained. Headache and early signs of increased intracranial pressure are the commonest clinical features. The waterlogged, glossy appearance of the surrounding brain may help in the gross diagnosis of the lesion at the operating table. Complete surgical removal of the lesion, whenever feasible, combined with adequate streptomycin therapy should be the therapeutic method of choice. Children seem to have a better change of survival than adults.

The three patients who died were adults. For one a diagnosis of intrapontile glioma was made, but craniectomy in the left suboccipital area did not disclose a tumor at the angle. The patient was subjected to intensive x-ray therapy but died three months later, of the effects of intracranial hypertension. Autopsy revealed a sausage-shaped tuberculoma, which extended from the left cerebellar lobe to the pons, midbrain, cerebral peduncle, and thalamus on the left side. The other two postoperative deaths were from tuberculous meningitis. Both patients were Indians; they had the longest duration of symptoms, were hemiplegic and extremely emaciated on admission, and had the largest tumors. Both were given dihydrostreptomycin, and one had additional intravenous injections of glucosulfone sodium (Promin). One died 87 days, and the other 101 days, after operation.

Alpers, Philadelphia [A. M. A. Arch. Neurol. & Psychiat.].

Measurement of "Extracellular Fluid Space" in Infants by Equilibration Technic Using Inulin and Sodium Ferrocyanide. Philip L. Calcagno, George S. Husson, and Mitchell I. Rubin, Proc. Soc. Exper. Biol. & Med. **77**:309 (June) 1951.

Data collected from six infants 9 days to 14 months of age with severe congenital defects involving the central nervous system show a good correlation of "inulin" space when estimating both at the equilibrium period and after collection of totally excreted inulin. In these studies 5% dextrose solution containing 1% inulin and 0.01% sodium ferrocyanide was given as a constant intravenous infusion at the rate of 0.75 to 1.0 ml. per minute. Equilibration was designated as the period when a constant plasma level was obtained, which for inulin was within 2 hours and for sodium ferrocyanide within 45 minutes. The ratio between the sodium ferrocyanide and the inulin space was 1.04.

Hansen, Galveston, Texas.

Seasonal Incidence of Congenital Malformations of the Central Nervous System. T. McKeown and R. G. Record, Lancet **1**:192 (Jan. 27) 1951.

McKeown and Record report on the seasonal incidence of congenital malformations of the central nervous system, using as source material the annual reports of the Registrar-General

for Scotland for seven years and 930 consecutive cases of malformations of the central nervous system in Birmingham over a seven-year period. They found that of all malformations reported as stillbirths or first-year deaths, about 70 and 40%, respectively, involved the central nervous system. The incidence of anencephalus was significantly higher in children born in the half-year from October to March than in those born in the half-year from April to September. Although the risk of anencephalus is higher for first than for later births, this factor was statistically ruled out as a likely cause for the seasonal variation. There was no evidence of seasonal variation in the incidence of spina bifida or hydrocephalus.

The authors also found that the incidence of malformations of the central nervous system in siblings born after the birth of a child with such a malformation is about six times the expected rate.

MADOW, Philadelphia [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

REHABILITATION OF THE CEREBRAL PALSY CHILD. M. MEDALIE, South African M. J. **26:** 569 (July 12) 1952.

The Forest Town School, at Johannesburg, has been in operation for three years. Admission is limited to educable children, and these are admitted as young as 2 years. The basic policy is one of treating the child as a whole psychobiological organism. Treatment involves physical therapy, speech therapy, and educational and emotional development. These phases are well coordinated by members of the staff. The various phases are outlined in some detail. Results have been good. It is stressed that early treatment is important for best results.

McGUIGAN, Evanston, Ill.

INTRACRANIAL HYPOTENSION: REPORT OF 23 OBSERVATIONS WITH THEORIES CONCERNING HYPOTENSIVE STATES. P. GLOOR, Schweiz. med. Wchnschr. **81**:326 (April 7) 1951.

There is no definite clinical picture of intracranial hypotension, that is, conditions in which the pressure of the cerebrospinal fluid is abnormally low and in which the ventricles are collapsed. A case is cited in which the left ventricle was collapsed and the patient manifested a right hemoplegia and aphasia. On injection of air into the ventricle all signs disappeared. The hypotensive states are divided into several groups. Some observations in children are of interest. A 12-year-old girl suddenly had an epileptic attack ending in coma from which she emerged with a left flaccid hemiplegia and a Babinski sign. When a needle was introduced into the ventricle no fluid was obtained before injection of air. Fifteen minutes after filling of the ventricles with air recovery was complete. In a 10-year-old girl with a diagnosis of tuberculous meningitis the cerebrospinal fluid pressure was diminished. There was no block. For further detail the paper has to be consulted.

AMBERG, Rochester, Minn.

REGITIN (PREPARATION C7337) A NEW IMIDAZOLDERIVATIVE WITH SPECIFIC SYMPATHICOLYTIC ACTIVITY. F. GROSS, J. TRIPOD and R. MEIER, Schweiz. med. Wchnschr. **81**:352 (April 14) 1951.

The pharmacological activity of Regitin (2[N-*p*'-tolyl-N-*m*-oxyphenylaminomethyl]imidazole) is reported. The compound inhibits many reactions of epinephrine and artenerol in concentrations which do not elicit its own activity.

AMBERG, Rochester, Minn.

THE GENESIS OF FEVER CONVULSIONS IN CHILDHOOD. K. LENGGENHAGER, Schweiz. med. Wchnschr. **82**:385 (April 12) 1952.

The volume of the lung in relation to the body mass is smallest in early childhood. With increasing age, the volume of the lung increases absolutely and relatively. A too small volume of the lung must elicit the same mechanism as the respiration of the adult at high altitudes, when the basal metabolism is raised (fever or erogenous elevation of body temperature). Thus, the respiratory volume has to be increased, resulting in hyperventilation alkalosis with its consequences, such as convulsions, in the presence of hyperthermia. The various factors by which this is brought about are enumerated. The fever convulsions correspond to the convulsions of heat stroke in adults. It is not necessary to assume any relation with epilepsy.

AMBERG, Rochester, Minn.

FOUR CASES OF ACUTE TRANSITORY HEMIPLEGIA. I. SALA, Lattante **24**:175 (March) 1953.

Each of four children, aged 10 months to 5 years, had a high-grade fever, a severe convulsion, and coma, which were followed by hemiplegia. The temperature had fallen by the third day to normal, and the signs of hemiplegia had disappeared by the eighth day. At that time the reflexes on the two sides had become equal, and the children were able to walk in a normal manner. There was no abnormality in the cytology or in the sugar and protein contents of the spinal fluid. In a discussion of the differential diagnosis, an acute virus infection and an allergic cerebral edema were considered.

HIGGINS, Boston.

OTOSINAL FOCI IN PURULENT MENINGITIS IN CHILDREN. ENRIQUE DELUCCHI, Rev. otorrinolaring. **12**:54 (Sept.) 1952.

The author discusses purulent meningitis in children and stresses the importance of determining the latent focus of infection in either the ear or the sinuses. Most careful examinations should be made and supplemented by x-rays. In doubtful cases surgical exploration is advised. Adequate and early, intensive antibiotic treatment should be instituted. However, it must be remembered that many of these cases are due to a Pneumococcus organism which may make the symptomatology rather confusing. DeLucchi reports two groups of patients. In the group, of 21 children, who died of purulent meningitis, 10 of them revealed frank foci either in the ear or in the sinuses. In the group, of 15 children, who recovered from an attack of purulent meningitis, 8 of them had a positive focus and 4 others a doubtful focus in either the ear or the sinuses. In conclusion, he stresses the importance of early surgical intervention to avoid not only death but also many serious sequelae, such as cysts, blindness, deafness, hydrocephalus, and idiocy.

PERSKY, Philadelphia [A. M. A. ARCH. OTOLARING.].

PHYSICAL THERAPY IN INFANTILE CEREBRAL PALSIES. ALFONSO TOHEN ZAMUDIO and MARIA DE LA LUZ LEYTTE, Bol. méd. d. hosp. inf., México **7**:56 (Feb.) 1950.

The authors describe what may be understood by infantile cerebral palsy, and its causes. The incidence of this disease is 7 children per 100,000 population according to this report. Five clinical types are considered: spastic, athetotic, ataxic, rigid, and with tremors. A description is made of each type, and the lesions are pointed out. It is important to study children with infantile palsies from the psychologic point of view, in order to institute a more successful treatment.

The treatment may be divided into these categories: (*a*) physical therapy, (*b*) occupational therapy, (*c*) speech therapy, (*d*) apparatotherapy and (*e*) medicaments and surgery. Physical and occupational therapy differ according to the type of cerebral palsy. In general, it may be said that there are several points which are common to all: conditioned motions, massage, combined motions, rest, relaxation, balance, reciprocal motions, reaching for an object, seizing it, and releasing it, and the ability to execute several motions.

FROM THE AUTHORS' SUMMARY.

SPEECH PROBLEM IN INFANTILE CEREBRAL PALSY. CRISTINA BIENVENU H., Bol. méd. d. hosp. inf., México **7**:67 (Feb.) 1950.

In the efforts directed toward the rehabilitation of children affected with infantile cerebral palsy, the speech problem must not be overlooked. To attain a better means of locomotion without increasing the ability to speak only augments the inferiority complex of the child.

Not all children affected with infantile cerebral palsy have disturbances of speech, but many of them do. These children, in the majority of instances, have great possibilities of speaking intelligibly.

The progress is slow, and in order to be successful, not only the coordination of the physicians, the physical therapy technicians, and the professors in speech disturbances are required; it is also important to count on the cooperation of the parents.

Perfection is almost never reached with these patients, but anything done for them would help to improve their condition. A great mistake would be made if it were assumed that a

patient in that condition left to himself would in time learn to speak. Even in mild cases, the child needs the help of the teacher; otherwise, he would acquire defects in the enunciation of words which, as time passes, become increasingly difficult or impossible to correct.

From the Author's Summary.

Epidural Abscess in the Spinal Region in Childhood. A. Goes, Kinderärztl. Praxis **17**:315 (Sept.) 1949.

A discrepancy between the findings on lumbar puncture and those on puncture of the cisterna magna led to the diagnosis of epidural abscess with secondary meningeal infection caused by perforation of the abscess and introduction of the infected needle into the meningeal sack during the first lumbar puncture. Surgical opening of the abscess with drainage and sulfonamide and penicillin therapy led to cure of the patient.

Glaser, Jerusalem.

Special Form of Meningitis Due to Salmonella Panama. D. Gericke and H. Luchtrath, Med. Klin. **46**:862 (Aug. 19) 1951.

An infant 3½ months of age was taken acutely ill and exhibited meningeal signs which did not yield to penicillin or streptomycin. In the cerebrospinal fluid many lymphocytes were found; later the fluid became thickly purulent. From the spinal fluid Salmonella Panama could be isolated. The family lived at the time at which infection could have taken place in a region where S. Panama infection was not infrequent. Hence the infection could have been direct or by way of the parents. At postmortem examination, in addition to other lesions, a severe purulent meningitis of the lymphocytic type over the convexity was found extending in places to the base of the brain. Pronounced production of adventitia and pia cells with special capacity for phagocytosis was seen. The brain itself was the seat of marked encephalitis.

Amberg, Rochester, Minn.

Treatment of Petit Mal with Tridione. L. de Leener, Acta pædiat. belg. **2**:62, 1948-1949.

The author reports on two patients with epilepsy treated successfully with intermittent courses of trimethadione (Tridione). The first child, 13 years of age, had had petit mal seizures beginning at 6 months of age and consisting of loss of consciousness, twitchings of lid and eye muscles, lasting 5 to 30 seconds and occurring at the rate of 30 to 50 per day. After unsuccessful treatment attempts by other means, trimethadione in doses of 300 mg. three times a day for 10 days with a rest period of 10 days, followed by a second course of trimethadione was attempted and led to practical disappearance of seizures (one seizure every 8 to 10 days). Because of unavailability, administration of the drug had to be discontinued for seven weeks and no recurrence of attacks was noted. From then on intermittent courses of trimethadione were given with gradual prolongation of the intervals with the same beneficial effect.

A similar beneficial effect was obtained in a 10-year-old child who had had seizures since the age of 2 years, following encephalitis. The author believes that the two cases are worth reporting because of the absence of seizures between treatment courses, pointing toward a possible curative as well as a symptomatic effect of the drug.

Glaser, Jerusalem.

A Contribution to the X-Ray Diagnosis of Sympathicoblastoma with Special Regard to the Skeletal Changes. J. Houstek, Z. Hlouskova, and A. Rubin, Pediat. listy **6**:328, 1950.

The x-ray changes in 12 cases of sympathicoblastoma are described. The thoracic sympathetic was the first site of the tumor in three children and it was affected in another two cases in conjunction with the abdominal sympathetic. The pyelogram was typical in four cases, with distal and lateral displacement of the kidney; in two cases the findings were completely negative, and in the remaining cases the changes were not characteristic (enlargement of the pelvis and calices and axial rotation). Calcification was found in 50% of the patients.

The skeletal changes in repeated examinations were not characteristic in three children and were well defined in nine. The bone metastases were of a combined osteoplastic and osteoclastic type in three patients; in the remaining cases they were purely osteoclastic.

FROM THE AUTHORS' SUMMARY.

WIDESPREAD DEMYELINATION IN CHILDREN. K. BRACHFELD, J. HOUSTEK, I. LESNY, and J. SVATY, Pediat. listy **7**:273, 1952.

Ten cases of widespread demyelination in children were observed. In two the diagnoses were confirmed post mortem; in the remaining cases diagnosis was made on clinical findings. The symptomatology is presented in tables. The frequency of cerebellar signs (4 cases), changes on the papilla (4 cases), and mainly the increase of protein in the cerebrospinal fluid are stressed. Little attention has hitherto been given to the latter. The authors are convinced that demyelination must be distinguished from degenerative, perineal, and inflammatory diseases. Diseases of demyelination form a separate and definite neurological group.

FROM THE AUTHORS' SUMMARY.

Psychology and Psychiatry

CRITICAL EVALUATION OF THE PRESENT STATE OF CHILD PSYCHIATRY. DAVID M. LEVY, Am. J. Psychiat. **108**:481 (Jan.) 1952.

Levy presents a review of the history of the child guidance clinic and its influence on child psychiatry in this country.

JAHR, Omaha.

PARENTAL DEPRIVATION AND THE "BROKEN HOME" IN DEMENTIA PRECOX AND OTHER MENTAL DISORDERS. JANE E. OLTMAN, JOHN J. MCGARRY, and SAMUEL FRIEDMAN, Am. J. Psychiat. **108**:685 (March) 1952.

According to this report, there is no significant difference in the incidence of parental deprivation among patients suffering from dementia praecox, manic-depressive psychosis, alcoholic state, and "other psychoses." Parental deprivation was considerably higher among psychoneurotic and psychopathic personalities.

JAHR, Omaha.

AN EVALUATION OF GLUTAMIC ACID IN MENTAL DEFICIENCY. RALPH N. ZABARENKO and GUINEVERE S. CHAMBERS, Am. J. Psychiat. **108**:881 (June) 1952.

A group of 58 mentally defective patients (mainly imbeciles) were studied. Glutamic acid failed to produce any significant gain in mental functioning.

JAHR, Omaha.

CLINICAL ASPECTS OF CHILDHOOD SCHIZOPHRENIA VIEWED FROM INTEGRATION LEVELS. I. M. MARCUS, New Orleans M. & S. J. **104**:541 (July) 1952.

Recognizable clinical aspects of childhood schizophrenia are reviewed. The author states that all mental activity is a product of underlying brain structure, and consequently whether childhood schizophrenia is symptomatic or genuine will depend on whether the disturbance is produced by known agents or by spontaneous electrochemical changes which cannot be demonstrated by present means. Alteration in brain function may be produced by organic disease, certain drugs, severe emotional stress, or congenital brain dysfunction.

MCGUIGAN, Evanston, Ill.

PUNISHMENT AND THE MALADJUSTED CHILD. RICHARD W. B. ELLIS, Canad. M. A. J. **67**:209 (Sept.) 1952.

In a learned and logical paper on the maladjusted child, the effect of punishment is considered. It is pointed out that when the parent-child relationship is unsatisfactory and the child feels himself unloved and rejected by one or the other parent, punishment assumes a much

more frightening and damaging role. It is apparent that when the parent-child relationship is satisfactory punishment is likely to be the most effective and least often necessary. When the child feels insecure and unloved, punishment fails because it is interpreted as one more evidence of parental hostility. This attitude leads to repeated and excessive punishment, with a defiant or "don't care" reaction from the child. This reaction is the child's defense against the basic lack of parental affection. Pushed too far, this attitude becomes one of rebellion against society as a whole and results in a socially maladjusted adult.

McGuigan, Evanston, Ill.

Congenital Universal Indifference to Pain: A Case Report. M. Cerny-Waldvogel, Ann. paediat. **178**:65 (Feb.) 1952.

The patient discussed by the author was affected by a congenital, generalized indifference to pain. Short reference is made to all cases in the literature as far as they were known to the author. The mechanism of insensitiveness to pain in congenital universal indifference to pain which Schilder and Stengel considered to be indifference toward the painful experience and called "asymboly" is discussed, but in the author's opinion other causes were responsible for the symptoms in their cases.

An attempt was made to localize the disturbance in the mechanism of pain conduction, and it was thought due to a developmental, error-like, congenital word deafness and word blindness which are considered to be selective developmental defects. Thus the hypothesis of "asymboly" becomes redundant for these cases. On account of this defect, the psychological event "pain" does not take place; although the afferent path of pain stimulus from the periphery persists, pain is not experienced.

From the Authors' Summary.

Child Guidance Clinic: An Essential Factor in the Therapeutic Field of Psychological Disorders. J. Stroeder and W. Günter, Arch. Kinderh. **141**:65, 1951.

This is a symposium dealing with the historical development of the child guidance clinic in United States of America. The authors emphasize the importance in the future of similar institutions in Germany and discuss the problems of cooperation between pediatricians and psychiatrists, the dangers of specialistic limitations, and the problems of organization.

Gottstein, Chicago.

Diseases of Genitourinary Tract

Histophysiology of the Fetal and Infantile Ovary. J. A. Rodriguez-Soriano, Arch. pediat. **10**:441 (Jan.) 1952.

The author, who has spent 10 years studying the histopathology of the ovary, traces the histologic changes in the fetal ovary, endometrium of the uterus, and vaginal epithelium and compares such changes with those in the newborn infant and in the child up to puberty. The ovary in the last three months of fetal life and up to 10 years is not a histological gland in a state of complete inactivity but rather presents activity of growth and concomitant atresia of primordial follicles. The author believes that this is not a simple disappearance of the primordial follicles but is a growth and regression which is like an anovular cycle. True corpoa lutea are not formed but there are changes in the endometrium suggestive of a cycle not accompanied by ovulation. The author believes that hormones and other stimulating substances should be used with great caution if at all.

Allen, San Francisco.

Chronic Renal Disease in Children. Harry H. Boyle and Edwin F. Hirsch, Illinois M. J. **102**:214 (Sept) 1952.

Boyle and Hirsch report two cases and present a general discussion of chronic renal disease in children.

Barbour, Peoria, Ill.

THECA-CELL TUMOR OF OVARY IN CHILD ONE YEAR OF AGE. VIDA H. GORDON and HORACE N. MARVIN, J. Pediat. **39**:133 (Aug.) 1951.

Gordon and Marvin review the literature and report a theca-cell tumor of the ovary in a one-year-old infant. There was a white vaginal discharge and, later, vaginal bleeding. Uterus, breasts, and labia minora were enlarged. The excretion of 17-ketosteroids was 0.05 mg. in 24 hours, and of estrone in the urine, 230 I. U. After removal of the tumor, vaginal epithelium which had been cornified regressed to the infantile state. MACDONALD, Pittsburgh.

PORPHYRIA IN A CHILD OF EIGHT YEARS. V. BAFFI and L. DE SIENA, Pediatria **59**:726, 1951.

The authors describe a case of acute porphyria with abdominal symptoms which was successfully treated with the pellagra-preventive factors of the vitamin B complex during the acute phase. They review the most recent investigations concerning porphyrin metabolism.

FROM THE AUTHOR'S SUMMARY.

Diseases of Ductless Glands; Endocrinology

ANTAGONISTIC RELATIONSHIP BETWEEN TESTOSTERONE AND THYROXINE IN MAINTAINING THE EPIDERMIS OF THE MALE RAT. H. EARTLY, B. GRAD, and C. P. LEBLOND, Endocrinology **49**:677 (Dec.) 1951.

Recently, it was found that physiological amounts of testosterone and thyroxin were essential for the maintenance of the normal weight and histological picture of such organs as heart, kidney, hypophysis, and submaxillary glands in the male rat. In experiments reported by the authors, testosterone was found to increase and thyroxin to decrease the thickness of the epidermis in castrated thyroidectomized rats, while the joint action of the substances resulted in an intermediate thickness approximating that in intact animals.

It is concluded that, in addition to the well-recognized androgenic function of testosterone and metabolic function of thyroxin, these hormones may jointly act on a variety of end-organs, either additively, as on the hypophysis; synergistically, as on the heart, kidney, and submaxillary glands, or antagonistically, as on the epidermis. JACOBSEN, Buffalo.

EOSINOPHIL RESPONSE TO STRESS IN ASCORBIC ACID PRETREATED MICE. HABEEB BACCHUS and NORMAN ALTSZULER, Endocrinology **51**:1 (July) 1952.

Ascorbic acid treatment prevents the adrenal hypertrophy typical of animals exposed to cold and enhances the survival of animals exposed to this stressor. It was observed that ascorbic acid pretreatment prevented the eosinopenia and the depletion of adrenal cholesterol typical of acute epinephrine stress.

This paper reports data which indicate that ascorbic acid prevents the eosinophile response to epinephrine but not that to corticotropin.

These observations were interpreted as indicating that the vitamin operated in this mechanism by depressing the release of pituitary corticotropic hormone. JACOBSEN, Buffalo.

EXCRETION OF FORMALDEHYDEGENIC (FG) SUBSTANCES BY NORMAL AND SCORBUTIC GUINEA PIGS. ELI M. NADEL and JOHN J. SCHNEIDER, Endocrinology **51**:5 (July) 1952.

In this study the authors report data on the excretion of corticoid substances by the normal, the starved, and the scorbutic guinea pig. These data show that normal male guinea pigs excrete relatively large amounts of corticoids and that severely scorbutic animals excrete significantly greater amounts. The enhanced excretion of corticoids in the scorbutic state is of interest, for, although scurvy probably represents a severe stress situation for the guinea pig and elicits increased adrenal activity, the increased activity is manifest in a gland in which the ascorbic acid content is at very low levels. The evidence strongly suggests that in the guinea pig ascorbic acid is not necessary for the elaboration of adrenocortical hormones.

JACOBSEN, Buffalo.

THE EFFECT OF THYROIDECTOMY ON THE MORTALITY AND PERIPHERAL BLOOD CHANGES OF THE RAT SUBJECTED TO WHOLE BODY X-IRRADIATION. A. L. KRETCHMAR, H. J. GOMBERG, D. E. WEYANT, and F. H. BETHELL, Endocrinology **51**:59 (July) 1952.

The authors conclude from this study that irradiation leucopenia and anemia are severer and more prolonged in thyroprivic than in euthyroid animals.

JACOBSEN, Buffalo.

EFFECTS OF ADRENAL CORTICAL EXTRACT ON RENAL FUNCTION IN HYPOPHYSECTOMIZED RATS. W. R. BOSS, C. M. OSBORN, and ALFRED A. RENZI, Endocrinology **51**:66 (July) 1952.

Under the conditions of these experiments it seems apparent that the action of the hormone is primarily on the renal tubule reabsorption of water and of the electrolytes.

JACOBSEN, Buffalo.

EFFECT OF DESOXYCORTICOSTERONE ACETATE ON ELECTROLYTE METABOLISM IN A NORMAL MAN. PAUL FOURMAN, E. C. REIFENSTEIN, E. J. KEPAR, E. DEMPSEY, F. BARTTER, and FULLER ALBRIGHT, Metabolism **1**:242 (May) 1952.

Balance studies on a 24-year-old normal man revealed that a single injection of 30 mg. of desoxycorticosterone acetate produced the following results:

1. Loss of potassium, which was not accompanied by corresponding loss of phosphorus. This finding was interpreted as reflecting a change in composition of the intracellular fluid rather than a diminution in its volume.

2. Retention of sodium accompanied by retention of chloride without change in the concentration of these electrolytes in the plasma. This was interpreted as reflecting an increase in extracellular volume.

Since the duration of the period over which sodium was retained was greater than that over which potassium was lost, and since the magnitude of sodium loss was considerably greater than that of potassium gain, it was concluded that desoxycorticosterone acetate acts on these two substances independently. Some sodium did, apparently, become intracellular.

KAPLAN, Cincinnati.

DIABETICS IN PREGNANCY. A. F. ST. AMANT, New Orleans M. & S. J. **104**:660 (Oct.) 1952.

Complications of diabetes in pregnancy are listed as acidosis; preeclampsia; increased hypertension with albuminuria; excessive edema with hydrammios; obstetrical complications due to large babies, poor labor, and high incidence of breech presentation, and physiological immaturity of the infant despite excessive size.

These complications may result in fetal death at three periods; intrauterine death after 32 weeks when associated with maternal toxicity; intrapartum deaths due to accidents associated with delivery of large babies, stuck shoulders, and excessive traction, and neonatal deaths due to traumatic delivery, prematurity, and physiological immaturity of infants of diabetic mothers.

Care of the diabetes throughout the pregnancy is necessary to lower the infant mortality. Routine hospital admission at the 35th week for careful evaluation as to time and method of delivery is advised.

MCGUIGAN, Evanston, Ill.

DIABETES IN CHILDHOOD. J. A. AVANT, JR., New Orleans M. & S. J. **104**:662 (Oct.) 1952.

Premonitory signs of diabetes in children are frequently mild and easily overlooked. For this reason approximately 10% of diabetic children are first seen in a state of coma. To detect diabetes in an early stage, a constant awareness of diabetes is necessary. The long-term management of diabetes in children is necessarily difficult because of the rigid control needed over children, who must be taught cooperation. Here the emotional health of the child is

important and must be closely guarded. Brief mention is made of the care of the newborn of the diabetic mother. The points are made that such infants do not have a low blood sugar and that oxygen is of paramount importance.

, McGuigan, Evanston, Ill.

Iodine Prophylaxis and Iodine Deficiency Theory. Investigations Concerning the Thyroid Gland Conditions of School Children in Some Swiss Villages. H. J. Wespi, Schweiz. med. Wchnschr. **83**:452 (May 9) 1953.

The paper deals with the question whether goiter can arise in consequence of a deficiency in iodine, a theory which has been denied by some. Attention is called to a primary deficiency distinguished by (*a*) "exocarence," insufficient iodine content of food and water; (*b*) "enterocarence," perhaps an insufficient absorpition of organic iodides, and (*c*) "endocarence," increased demand of iodine under various conditions. A secondary deficiency may arise from disturbances of the utilization of iodine. Here also various subdivisions are given. The school children in some communities in the Zurich and Aargau Cantons had been investigated 40 and 20 years previously. In the Zurich Canton the frequency of goiter decreased from 47% in 1912 to 1% in 1952, and in the Aargau it dropped from 55% to 17%; in the Zurich Canton the use of iodized salt has been much more extensive than in the Aargau Canton. The effect is due to the correction of an iodine deficiency.

S. Amberg, Rochester, Minn.

The Weight of the Thymus in Children Under Two Years of Age. Hilkka Tahka, Acta paediat. **40**:469 (Nov.) 1951.

The thymuses of 309 children of 0 to 2 years of age who died from various diseases were weighed at autopsy. The individual variations in the size of the thymus are fairly great; in full-term infants 0.50 to 28.55 gm. and in prematurely born children 0.20 to 12.93 gm. Age has no clearly discernible influence on the weight of the thymus. During the last weeks of pregnancy the thymus seems to increase to some extent. There is no difference in the size of the thymus in relation to sex. The weight of the thymus decreases rapidly with prolongation of the duration of the disease. The size of the thymus depends evidently to a great extent on the nutritive condition of the child. Consequently, the smallest thymuses are found in children who have died of chronic gastroenteritis. There were no cases of the so-called "thymus-deaths." The average weight of the thymus and of the thyroid gland increase proportionately.

From the Author's Summary.

Diseases of Muscles, Bones, Joints, and Lymph Nodes

Multiple Congenital Malformations of the Skeletal System: A Case Report. Everett J. Gordon, Nathan Shechter, and Aaron W. Perlman, Am. J. Roentgenol. **59**:533 (April) 1948.

The case presents numerous congenital skeletal defects which, when combined, cannot be classified properly as belonging to any known entity. The outstanding skeletal malformations are multiple luxations, involving both patellae and both radiohumeral joints, and multiple instances of congenital type fusion of small bones, involving the carpals of both wrists and the cervical spine and the lumbar spine. Slighter deformities of both feet and the skull are observed. The author gives a brief discussion of the theories advanced in explanation of such malformations.

Harrison, Oak Park, Ill.

Chondrodystrophy and Mental Defect. W. P. N. Jackson and C. L. B. Jeppe, South African M. J. **26**:541 (July 5) 1952.

A case of chondrodystrophy in a mentally defective child is described. While not typical, the patient presented several features suggestive of gargoylism. The authors feel that this is probably an instance of atypical gargoylism.

McGuigan, Evanston, Ill.

CLUTTON'S SYNOVITIS AND PENICILLIN. JORGE ROSSELOT, Rev. chilena pediat. **22**:147 (April) 1951.

The bibliography on Clutton's joints is reviewed, and the clinical histories of two cases in which penicillin was used are presented. The patients were boys of 3 and 13 years of age who had bilateral hydroarthrosis of the knees, with negative x-ray findings and mild localized pain.

The diagnosis of late congenital syphilis was verified by a positive Kahn test and some stigmata but no signs of specific activity. With penicillin therapy the slight localized tenderness rapidly disappeared, and in a follow-up investigation one year after treatment there was no articular swelling and there had been no relapse; in one of the patients the Kahn test had become negative, while in the other there was a questionable nonspecific positive reaction.

FROM THE AUTHOR'S SUMMARY.

TREATMENT AND PROSPECTS OF HEALING MAXILARY OSTEOMYELITIS OF INFANTS. WALTER ECKEL and WILHELM KOSENOW, Med. Klin. **49**:1299 (Dec. 7) 1951.

Removal of pus at the proper time by incision, or enlargement of existing fistulae, together with simultaneous sulfonamide-penicillin therapy over a sufficiently long period is given as the treatment of choice. Teeth buds should be removed only when absolutely necessary.

AMBERG, Rochester, Minn.

THE APPEARANCE OF OSSIFICATION CENTERS IN THE SKELETON OF THE HAND FROM BIRTH TO PUBERTY, WITH SPECIAL CONSIDERATION OF THE SESAMOID BONES OF THE HAND. ST. DEGEN, Med. Klin. **50**:1330 (Dec. 14) 1951.

The ossification of the sesamoid bones of the hand was studied in 67 boys and 87 girls.

AMBERG, Rochester, Minn.

MANDIBULAR FACIAL DYSOSTOSIS: A NEW SYNDROME OF "MULTIPLE DEGENERATION." H. WEYERS, Acta paediat. **40**:143 (March) 1951.

On the basis of his own observations the author describes a hereditary disturbance of the jaw and face area, which is to be regarded as a differentiation defect of certain zones of the tissues of the first branchial cleft and which shows in its development a characteristic picture which has been described by Franceschetti and Zwahlen (1944) under the designation of "dysostosis mandibulofacialis."

The complex of mandibular-facial symptoms is recognizable by a pronounced disposition of the organs and is manifested by macrostomia, microtia, and micrognathia, as well as by defects of the temporal orbit walls and their soft tissue covering. These deformities are caused chiefly by hypoplasia of the zygomatic bone and lead to an antimongolian direction of the eyelid axis.

Besides the changes in the bone of the face, there are anomalies of the thorax, dysplasia of the lungs, and malformation of the spinal column and the extremities, which indicate a generalized tendency toward malformation of the mesodermal tissue in addition to the above-described cranial abnormalities.

There are standard types showing all the above symptoms, "formes frustes" and one-sided localizations of the mandibular-facial process, as well as the extreme basic form, which is to be regarded as frequent as otocephalus in quadripeds. In cases with hereditary taint abortive forms also occur in conjunction with the full clinical picture, but sporadic cases have also been observed.

Clinical and pathological-anatomical findings suggest that this disease manifests itself about the seventh week of gestation and that it is related to the Klippel-Feil complex of symptoms, but that it can be distinguished in general as a separate biotype from other degenerative dystostoses.

FROM THE AUTHOR'S SUMMARY.

Diseases of Eye

AN EPIDEMIC OF ACUTE CATARRHAL CONJUNCTIVITIS. M. TERNI; V. PONS, and V. RIZZINI. Gior. mal. infett. and parassit. **4**:279 (Sept.) 1952.

A description is given of an epidemic of catarrhal conjunctivitis occurring among pupils and teachers of an elementary school near Florence. A total of 181 cases occurred over a period of seven weeks; 47 of the pupils were treated at the University Eye Clinic. Bacteriological and serological studies indicated that the etiologic agent was a Staphylococcus.

HIGGINS, Boston.

Cutaneous Diseases; Allergy

MIXED GRASS POLLEN VS. PURE TIMOTHY EXTRACT IN UNCONTROLLED SUMMER HAY FEVER PATIENTS. LOUIS STERNBERG, J. Allergy **23**:163 (March) 1952.

The author believes that about 20% of summer hay fever patients respond poorly when treated with timothy extract alone. A large number of those doing poorly were benefited when treated with an extract containing a mixture of timothy, sweet vernal, red top, June, orchard, and Bermuda grasses. Some of those who did poorly with pure timothy extract, manifested constitutional symptoms when given the extract of mixed grasses. Others gave more marked skin reactions to the other grasses than to timothy. These factors would indicate that the grass mixture contains specific antigenic factors not present in the timothy extract. The author's experience would suggest the routine use of an extract containing a mixture of grasses in the treatment of summer hay fever.

HOYER, Cincinnati.

ACRODYNIA FOLLOWING INGESTION OF MERCURIAL OINTMENT. FREDERIC N. SILVERMAN and HAROLD A. CASSADY, New England J. Med. **247**:343 (Sept. 4) 1952.

The authors report two cases of mercury poisoning in children, with resulting clinical manifestations of acrodynia. The source in both cases was ammoniated mercury ointment, but physicians are reminded that teething powders and diaper rinses may contain mercury.

In one patient the developing anlagen of the permanent teeth were destroyed and extensive orthodontic manipulation was required. Attention is directed toward the possible necessity for early prophylactic dental care. The second child was treated with dimercaprol (BAL), and increased renal excretion of mercury was noted.

These and other reported cases lend further support to the thesis that acrodynia is indeed a heavy metal poisoning.

WHEELOCK, Denver.

THE CARE OF INFANTILE ECZEMA. A. V. STOESSER, New Orleans M. & S. J. **104**:677 (Oct.) 1952.

The author outlines the more important and most practical features of all treatments for infantile eczema. Since the article consists in detailed descriptions of such treatments almost entirely, it does not lend itself to abstracting. It is a very useful article and should be read in its entirety.

THE POSSIBLE RELATIONS OF ACRODYNIA TO MODIFICATIONS OF VITAMIN B. R. CORDA, Ann. ital. pediat. **5**:357 (Oct.) 1952.

After summarizing the several pathogenetic theories on acrodynia, the author relates amply the connection that may be seen in the clinical and experimental field between this disease and action of the B group of vitamins. According to the data from literature and the therapeutic results in one case with the administration of some vitamin of the B group, he is led to regard Feer's disease as a syndrome in which several toxic infectious and vitamin deficiency factors may blend together in one terminal mechanism.

FROM THE AUTHOR'S SUMMARY.

EXFOLIATIVE DERMATITIS AFTER HYDANTOIN THERAPY. I. HATZMANN, R. NEUHOLD, and W. VON RITTNER, Ann. paediat. **179**:305 (Nov.) 1952.

A fatal case of exfoliative dermatitis after diphenylhydantoin treatment is reported. The importance of exact clinical observation is pointed out, and the necessity to pay attention to an existing disposition to inflammatory skin reactions or to past viral infection with skin manifestations such as measles and chicken-pox.

FROM THE AUTHORS' SUMMARY.

NEW CASES OF ECTODERMOSIS PLURIORIFICIALES OF FEISSINGER RENDU (STEVENS-JOHNSON'S SYNDROME). JERÓNIMO POU DIAZ, Acta pediat. españ. **7**:1241, 1949.

The disease starts abruptly and tumultuously with headache, high fever, and general toxic symptoms, after which the lesions appear on the skin and mucous membranes and ocular symptoms develop. The cutaneous lesions are polymorphic. There are papules, macules, and vesicles which rupture easily, leaving grayish hemorrhagic crusts. The mouth and eyes are always affected. The vagina, anus, and penis are less often involved. The skin lesions may be noted on the neck, extremities, and face but are rare on the chest or abdomen. The lesions around the mouth and eyes are synechial, but discrete lesions coexist with confluent ones.

The lips and the area around the eyes become badly swollen, reddened, fissured, and hemorrhagic. Frequently the lesions become ulcerated, with pseudomembranous scars. In ocular cases, according to Duke-Elder, there may be a simple conjunctivitis but in more serious cases panopthalmia may follow and even blindness may be a sequel of this strange disease.

The mouth and lips are similarly affected, the gums bleeding on the slightest touch. The buccal cavity, pharynx, and larynx may be invaded. The author says that in one case he had seen the trachea involved and a pseudomembranous cast of the bronchial tree actually expelled. In these cases, needless to say, the breath has a fetid odor.

Histologically the lesions are not specific but have the appearance of ordinary pemphigus and other bullous forms of dermatitis.

Various etiological factors have been thought responsible, such as (1) toxins, (2) allergy, (3) bacteria, (4) physical agents, (5) virus, and even (6) tuberculosis. The virus and allergic origins have been held to be most tenable. Further support is given to the allergic theory by the constant finding of eosinophilia and by the reports by Schoemperlen of cure or relief from diphenhydramine (Benadryl).

ALLEN, San Francisco.

SEBORRHOEIC DERMATITIS IN THE INFANT. JORGE ROOSELOT and RODOLFO BURDACH, Rev. chilena pediat. **23**:369 (Sept.) 1952.

The most important clinical features of 33 infants with seborrheic dermatitis are analyzed. Most of these were under 3 months of age, and all suffered from a deficient nutritional status. The most frequent lesions were the erythematodesquamative ones. In 12 infants the culture taken from the scalp and the skin of the abdomen was not different from that of a control group, the most frequent organism found, being the nonhemolytic Staphylococcus albus. The histopathologic picture in 20 patients revealed acanthosis, parakeratosis, hyperkeratosis, edema of the dermis, and cellular infiltration. Treatment was both local and general, with lubricants or astringents, vitamin B_{12}, parenteral penicillin, or local aureomycin. It is difficult to evaluate a single therapeutic measure; 20 infants showed a complete disappearance of the lesions in an average of 50 days. The nutritional deficit present forced the authors to use special formulas for long periods. The weight curve, except in four cases, was unsatisfactory.

FROM THE AUTHORS' SUMMARY.

INTESTINAL ALLERGY. WOLFGANG TILING, Ztschr. Kinderh. **67**:261, 1949.

The author believes that in children with sprue-like symptoms allergy may play a role. By means of numerous roentgenograms of the intestinal mucosa visualized by barium filling he shows changes in intestinal motility and mucosal pattern when the barium is given suspended in a nonallergenic liquid (water or soy bean milk) and when it is suspended in unboiled cow's milk, which was proved to be allergenic to the subjects of the test.

GLASER, Jerusalem.

Surgery and Orthopedics

SYMPOSIUM ON PEDIATRIC SURGERY. L. E. STRANGE, L. C. SCHLESINGER, and M. D. TEITELBAUM, New Orleans M. & S. J. **104**:1 (July) 1951.

Three authors contribute papers on pediatric surgery. Strange discusses various surgical conditions, including tracheoesophageal fistula, esophageal atresia, intestinal atresia, imperforate anus, malrotation of the intestines, congenital diaphragmatic hernia, omphalocele, reduplications of the bowel, intussusception, pyloric stenosis, and urinary obstructions. Special attention is paid to pre- and post-operative care and fluid and electrolyte balance.

Orthopedic problems of childhood are discussed briefly by Lee Schlesinger. All the common conditions are listed, under the headings of congenital deformities, infections, trauma, paralytic involvements, and static involvements.

Roentgenology is discussed by Meyer Teitelbaum. He correlates the roentgenographic findings with the various conditions discussed by the preceding authors.

McGUIGAN, Evanston, Ill.

Miscellaneous

DIPLOMYCIN. J. VALL BANERES, Arch. pediat. **10**:513 (Jan.) 1952.

The author describes the new antibiotic, called diplomycin, manufactured in Germany and Denmark. Certain patients with tuberculous meningitis have been reported as cured by diplomycin after the failure of streptomycin and paraaminosalicylic acid to effect a recovery. The product is obtained from a filtrate of a broth in which a growth of the Diplococcus X5 had been cultivated. This Diplococcus was discovered and named X5 by Noster in 1945. Its morphology and other characteristics are similar to those of Streptococcus lactis.

The action of diplomycin in vitro and vivo are described, and applications to other clinical uses are suggested. The toxicity is very low, and it has the advantage over streptomycin of causing no noxious symptoms in the vestibular apparatus. The dosage schedules are given. A comparison of the results of treatment by Enell, Luzen, and Melin in Denmark and of treatment by the author and Jaso in Spain, with dosages and clinical and laboratory findings, is given. Whereas the results were not startlingly good in the cases reported in Spain, the author admits the possibility that the patients were treated only after failure of streptomycin and paraaminosalicylic acid and rather late in the course of the disease.

ALLEN, San Francisco.

REACTIONS FOLLOWING THE USE OF TERRAMYCIN TROCHES: A CONTROLLED STUDY. AUSTIN H. KUTSCHER, JACK BUDOWSKY, STANLEY L. LANE, and NEAL W. CHILTON, J. Allergy **23**:177 (March) 1952.

A controlled study of troche therapy with oxytetracycline (Terramycin) was done on 218 patients. Troches containing the drug were given to 143 patients; 53.2% of these had some untoward reactions. Troches with a placebo were given to 75 patients, and 10.7% of these had an untoward reaction. Multivitamin therapy and tripelennamine (Pyribenzamine) were given to some of the patients who received the oxytetracycline troches to study their prophylactic or therapeutic effect against the oropharyngeal or gastrointestinal reactions. It was felt that neither had any beneficial effect. The reactions were sufficiently severe in 14.7% of the cases to warrant cessation of treatment. The authors conclude that oxytetracycline troches should be used only when indicated, and that they should not be used promiscuously.

HOYER, Cincinnati.

STUDY OF DRUG ACTION ON MAMMALIAN CILIATED EPITHELIUM. JOHN V. SCUDI, EUGENE T. KIMURA, and JOHN F. REINHARD, J. Pharmacol. & Exper. Therap. **102**:132 (June) 1951.

Sections of rat trachea immersed in Ringer's solution maintained cilia activity for four hours or longer. When exposed to vasoconstrictor, antibacterial and antihistamine drugs, such as are used in the nasal passages, suppression or reduction of ciliary motion occurred with all the drugs used in approximate therapeutic strength.

At drug concentrations which stop ciliary activity there is invariably an extrusion of a globoid substance which appears at the ciliated surface of the cell. Under constant microscopic observation it was observed that these "globoid bodies" detached themselves from the ciliated cell surface and were continually propelled toward the center of the tracheal ring, newer "bodies" being formed meanwhile. A small number of these extrusions may form without apparent loss of ciliary function but the authors have never observed extensive formation of these "bodies" without total loss of ciliary beat.

Because of the appearance of the nasal mucosa during an acute attack of the common cold or hay fever, tracheal rings from sensitized guinea pigs were treated with specific antigen. No effect was observed. Nor did histamine itself have any action on the ciliated epithelial tissue. The results indicate that with a variety of drugs there is a distinct parallelism between the loss of motility and the formation of globoid bodies. The authors are inclined to interpret these findings as indicating that alterations in the permeability of the cell membrane lead to the extrusion of viscoid globoid bodies and these, in turn, prevent ciliary motion.

PILCHER, Cleveland.

ACUTE SALICYLATE POISONING IN CHILDREN. RICHARD POIRIER and R. CORBET, Canad. M. A. J. **67**:117 (Aug.) 1952.

Toxic results from ingestion of salicylates depend to a large extent on acid-base imbalance. This imbalance is influenced by various factors. Salicylate poisoning stimulates cerebral centers, causing vomiting and also hyperventilation with resulting alkalosis. Salicylates also increase the metabolic rate, contributing to the depletion of glycogen, and their toxic effect on the liver can cause fatty degeneration. These two factors can cause severe and prolonged ketosis. Kidney function is depressed directly by a toxic effect and also by dehydration.

Treatment consists in combating dehydration and ketosis with large quantities of lactate and general supportive therapy.

McGUIGAN, Evanston, Ill.

THE BIOCHEMICAL INVESTIGATIONS IN PEDIATRICS. A. MUKHERJI, Indian J. Pediat. **19**:49 (April) 1952.

The author discusses briefly the various biochemical investigations used in pediatrics. The need for caution in evaluating these tests and the sources of variations are stressed. It is pointed out that no amount of chemical study can replace the need for careful clinical observation.

McGUIGAN, Evanston, Ill.

BIOCHEMICAL AND CLINICAL EFFECTS OF A NEW PREPARATION OF THE ADRENOCORTICOTROPIC HORMONE (ACTH). MUSSO R. BORTH and R. S. MACH, Schweiz. med. Wchnschr. **82**: 629 (June 14) 1952.

The new Ciba adrenocorticotropic preparation (Cibacthen) was tried for its anti-inflammation and antiallergic effect in a few patients with various diseases and in three with hypopituitarism of the anterior lobe of the hypophysis. In these cases the effect was good.

AMBERG, Rochester, Minn.

THE SULFONAMIDES. RITA MONTAGNA-GUERZONI, Lattante **20**:705 (Dec.) 1949.

This article is a review of the present day knowledge of the sulfonamide drugs, with discussion as to the mode of chemotherapy, the listing of the several sulfonamide drugs, and the pharmacology and therapeutics of each.

HIGGINS, Boston.

STATISTICS REGARDING NEOPLASMS OBSERVED IN THE CHILDREN'S HOSPITAL OF BRESCIA DURING THE YEARS 1942-1951. A. PAGANI-CESA and F. SCOLARI, Lattante **23**:343 (June) 1952.

Two hundred fifty-eight children with tumors were found among the 42,827 children admitted to the Children's Hospital at Brescia during the 10-year period 1942-1951. Fifty per cent of

the tumors were hemangiomata, 14% fibroadenomata (rectal polyps), 10% endocranial, and 4% renal tumors. The hemangiomata were found twice as frequently in the girls as in the boys.

HIGGINS, Boston.

USE OF CYTOTOXIC ANTIRETICULOENDOTHELIAL SERUM OF BOGOMOLETS IN DYSTROPHIC AND PREMATURE CHILDREN. L. MEINI, Lattante **23**:538 (Sept.) 1952.

When five dystrophic and one premature infant were given injections of the Bogomolets antireticuloendothelial cytotoxic serum, they gained weight and showed general clinical improvement. No untoward reactions to the serum were observed.

HIGGINS, Boston.

INTOLERANCE TO PENICILLIN. G. CEMBRANO, Lattante **24**:187 (March) 1953.

A four-year-old boy, with a history of eczema as a baby, had received injections of procaine-pectin-penicillin intramuscularly once each for three different illnesses about one year apart. After the first two injections, there had been localized edema and erythema and arthralgia lasting for about one week. After the third injection, the reaction was much more intense; in addition to the joint pains, there was marked edema of the buttocks and legs, with a vesicular eruption and a bronchitis. The child received relief from antihistamine drugs. He had eosinophilia (10%) in the peripheral blood. Skin tests were later made and were positive to penicillin, but negative to procaine and to pectin.

HIGGINS, Boston.

PHARMACOLOGICAL STUDIES ON THE HYDRAZIDE OF ISONICOTINIC ACID. G. RICCI, T. COPAITICH, and D. CURATOLO, Pediatria **60**:300, 1952.

The amount of the drug isoniazid (hydrazide of isonicotinic acid) found in the blood is proportional to the amount of which has been given by mouth. A dose of 2 mg. per kilogram of body weight every eight hours will maintain a satisfactory blood level. When an oral dose of 2.8 mg. per kilogram of body weight was given to a patient with pleurisy with effusion, a concentration of 0.6 γ per cubic centimeter was found in the pleural fluid two and one-half hours later. When the drug has been given intrathecally to patients with tuberculous meningitis, oral administration is also necessary to maintain a satisfactory therapeutic level in the spinal fluid.

HIGGINS, Boston.

BLOOD, SPINAL FLUID, and URINARY LEVELS OF VIOMYCIN. ALVARO MASI and PIERO MOGGI, Riv. clin. pediat. **49**:865 (Dec.) 1952.

The authors titrated blood, spinal fluid, and urine concentrations of viomycin after one oral dose of 20 mg. per kilogram and several intramuscular injections of 10 to 15 mg. per kilogram. Total doses of 30 to 60 mg. per kilogram and per day divided in three daily doses are sufficient for a tubercolostatic action.

FROM THE AUTHORS' SUMMARY.

POISONING WITH HYPNOTICS TREATED WITH PERVITIN (METHAMPHETAMINE HYDROCHLORIDE). CHRISTAZUR VERTH, Deutsche med. Wchnschr. **76**:806 (June 15) 1951.

A number of patients who had taken large although not fatal doses of hypnotics such as barbital sodium or cyclobarbital responded to intravenous injections of Pervitin (methamphetamine hydrochloride) much better than to pentylenetetrazol or nikethamide. One of the cases was that of a child 11 years of age, who received 0.5 ml. of Pervitin given 24 hours after unsuccessful nikethamide medication with immediate response. The child had received by mistake 1 gm. of barbital sodium.

AMBERG, Rochester, Minn.

PENICILLIN DOSAGE IN CHILDHOOD. F. K. FRIEDERISZICK and G. DORER, Med. Klin. **46**:749 (July 6) 1951.

Water-suspended combined depot penicillin in an amount of 200,000 I. U. in 2 ml. of water assures in infants a therapeutically efficient level of penicillin in the blood. After injections of

depot penicillin in oil in an amount of 150,000 I. U., an efficient blood level is maintained for 48 hours; in an amount of 300,000 international units for three days it is maintained for 36 hours in children of school age. A dosage of 1,200,000 international units insures an efficient blood level for 72 hours.

AMBERG, Rochester, Minn.

RULE OF THUMB FOR DETERMINING THE DOSAGE OF DRUGS FOR CHILDREN. A. AUGSBERGER, Med. Klin. **47**:14 (Jan. 4) 1952.

From the formula of Clark, taking in consideration the surface of the body, a simple rule of thumb for determining the dosage of drugs for children past the first year of life is derived; it is $(4 \times \text{age} + 20)$ % of the adult dosage. In this way empirically found correct doses were obtained for sulfonamide compounds, hypnotics, vermifuges, sympathomimetic agents, belladonna, and cardiac glucosides.

AMBERG, Rochester, Minn.

IN VITRO EXPERIMENTS ON THE CLINICAL APPLICATION OF STREPTOMYCIN AND PENICILLIN COMBINATIONS. I. GATTUNG, Ztschr. Kinderh. **69**:26 (No. 1) 1951.

The author studied the inhibitory effect upon the growth of Pneumococcus, Bacterium coli, Staphylococcus aureus, and hemolytic streptococci of combinations of penicillin and streptomycin solutions in various concentrations soaked in small pieces of filter paper and placed on the culture medium. It was found that if the solutions were used in sufficient concentration a synergistic effect could be observed, thus justifying the combined use of the drugs clinically if each one is administered in sufficiently high doses. No antagonistic effect could be noted.

GLASER, Jerusalem.

SIMPLE MICROCHEMICAL METHOD FOR DEMONSTRATION OF BARTITURATES IN THE CLINIC. H. KRESBACH and H. GOMAHR, Wien. klin. Wchnschr. **63**:476 (June 29) 1951.

A pure and absolutely water-free chloroform extract from urine, cerebrospinal fluid, and blood must be prepared. After addition of pyridine to 0.5% the extracts are evaporated to 0.5 ml. Special directions are given for obtaining usable extracts from blood. A drop of 1% cobalt nitrate in absolute methanol is placed on filter paper. After drying the extracts are added. After drying shortly the paper is exposed to ammonia vapors. In the presence of barbiturate a blue-violet color appears. Barbital could be determined in amounts of 1 to 2 γ, phenobarbital 5 to 10 γ, and pentobarbital 10 to 20 γ. The method proved of advantage in a number of cases.

AMBERG, Rochester, Minn.

CONTRIBUTION TO THE STUDY OF PENICILLIN: ITS USE IN INFANTS; METHODS OF ADMINISTRATION AND DOSES. R. DARTEVELLE, Acta pædiat. belg. **2**:151, 1948-1949.

The author studies blood levels obtained in infants from 2 days to 7 months of age treated with oral and intramuscular penicillin. He found that adequate blood levels (tested by bacteriostatic action against Staphylococcus aureus) can be obtained by oral administration of 50,000 units every eight hours to infants between 2 and 16 days of age. For children between 2 and 6 weeks of age 4 to 5 doses of 50,000 units in 24 hours must be given, and children from 6 weeks to 7 months must receive 5 doses in 24 hours. Aqueous crystalline penicillin given intramuscularly is rapidly eliminated and has to be given at frequent intervals and is therefore inferior to the oral preparation. The intramuscular administration of penicillin in oil and wax in adult doses to older children and in half of the adult doses to infants below one year produces adequate blood levels for 24 hours.

GLASER, Jerusalem.

HYALURONIDASE IN PEDIATRICS. J. HOFMAN, Pediat. listy **6**:350, 1951

The administration of hyaluronidase in saline hypodermoclyses in pediatrics is discussed. The solutions are rapidly absorbed without serious local reactions. The possibility of the similar use of hyaluronidase in other branches of medicine is considered.

FROM THE AUTHOR'S SUMMARY.

ARSENIC-STRYCHNINE INTOXICATION IN CHILDREN. HERBERT ENELL, Svenska läk.-tidning. **49**:628 (March) 1952.

Two siblings, 1 and 2½ years old, were found by the mother playing with drugs that had been given to the parents. One of these drugs contained arsenic and strychnine in red-coated tablets, 0.5 mg. of arsenic and 0.5 mg. of strychnine. The exact number of tablets taken is not known. An hour later the children fell ill with convulsions, cyanosis, and vomiting and became unconscious; the younger child died some hours later; the older child recovered. It is considered that two tablets of this compound were sufficient to cause fatal intoxication in infants.

WALLGREN, Stockholm, Sweden.

DANGER FROM TOYS. M. C. COLENBRANDER, Maandschr. kindergeneesk. **20**:328 (Nov.) 1952.

Giving a clinical description of three cases, the author discusses the consequences of dangerous toys. Nearly every week a child with a serious eye injury is admitted into his eye clinic. Therefore such toys should be absolutely forbidden, but at the same time one must provide other harmless outlets for the child's aggressiveness.

FROM THE AUTHOR'S SUMMARY.

News and Comment

GENERAL NEWS

Specialists Certified by the American Board of Pediatrics, Inc.—The following physicians were certified as specialists by the American Board of Pediatrics, Inc., after examinations held at Ann Arbor, Mich., on June 26, 27 and 28, 1953:

Adler, Norman Nathaniel, Fort Eustis, Va.
Ainsworth, Louise Powers, Columbus, Ohio.
Anderson, Ray Carl, Minneapolis.
Berg, George Shepard, Lt., (MC), U. S. A.
Berg, John William, Ames, Iowa.
Bergstrom, William Hugo, Syracuse 10, N. Y.
Boersma, Vernon L., Holland, Mich.
Borges, Wayne Howard, Cleveland Heights.
Brodsky, Emanuel David, Harrisburg, Pa.
Brown, Harold Zelig, Los Angeles.
Calodney, Martin H., Clayton, Mo.
Costello, Paul Joseph, Manchester, N. H.
Dawson, Katherine E., Columbus, Ohio.
Edelman, Samuel A., White Plains, N. Y.
Elghammer, W. Robert, Danville, Ill.
Eubank, David Furman, Chicago.
Feinauer, Lyman R., Salt Lake City.
Fijan, Kenneth J., Lincoln, Neb.
Fong, Willis M., Seattle.
Forer, Robert, Trenton, N. J.
Forney, John L., Bakersfield, Calif.
Frank, Max, Talmage, Calif.
Frank, Minnie, Chicago.
Gillick, Edward E., Jr., Niagara Falls, N. Y.
Gilmore, Robert L., Chicago.
Gormley, C. James, Plymouth, Mass.
Harris, Leon A., Beverly Hills, Calif.
Hauser, Donald Charles, Minneapolis.
Hudson, Phoebe, Wilmington, Ohio.
Kagay, Charles L., Dayton, Ohio.
Kalinowski, Aloysius A., Buffalo.
Katz, Benjamin E., Twin Falls, Idaho.
Kinsell, Clift Seybert, Santa Barbara, Calif.
Kolle, Fred Wynne, Wharton, Texas.
Krevsky, David A., Lincoln Park, Mich.
Ledis, Seymour, Lt., (MC), U. S. A. F.
Lendrum, Bessie Lieberman, Chicago.
Lerch, Theodore Trowbridge, Marysville, Calif.
Lewis, Philip Lewis, Denver.
Liebling, Wilbert, Los Angeles .
Lienke, Roger Irving, Iowa City.
Lissauer, Charlotte B., New York.
Lo Presti, Joseph Michael, Washington, D. C.
Luce, Ralph R., Seattle.
Lynn, James Wiley, Jr., Rochester, N. Y.
McMahon, William J., Niagara Falls, N. Y.
MacKinney, Loren Greenwood, Buffalo.
Matthews, Norman L., Marquette, Mich.
Mouton, Charles M., Los Angeles.
Muller, Richard P., Scott Air Force Base, Ill.
Newton, Joseph R., Fort Monmouth, N. J.
Orme, Harry William, Long Beach, Calif.
Pearce, Earl Barrie, Longview, Wash.
Peck, Charles Eugene, III, Euclid, Ohio.
Plummer, Lois J., Buffalo.
Post, David B., Albuquerque, N. M.
Rathkey, Arthur Stanley, Lt., (MC), U.S.A.F.
Reedy, Mary Ellen, Elmhurst, Ill.
Reichert, John M., Chicago.
Robin, Sidney W., Chicago.
Roth, Arthur, Oakland, Calif.
Sacks, Martin Oscar, Chicago.
Sapin, Samuel O., New York.
Schiff, Lester H., Niagara Falls, N. Y.
Seagle, Joseph Bowman, Champaign, Ill.
Shepard, Kenneth Sihler, Evanston, Ill.
Shibuya, Madoka, New York.
Shick, Paul Ellsworth, Jr., Portland.
Siebers, Bernard Herman, Grand Rapids, Mich.
Swift, Frank Louis, Fort Belvoir, Va.
Takenaka, Kameichi, Honolulu, T. H.
Trivette, Parks Dewitt, Hickory, N. C.
Veasy, Lloyd George, Salt Lake City.
Waldman, A. Martin, Wantagh, L. I., N. Y.
Washington, Edward L., Columbia, Mo.
Waterman, Donald Frederick, Grand Rapids, Mich.
Weil, William B., Jr., Cleveland.
Wetzel, Dick Davis, Tacoma, Wash.
Whitworth, Rex Hancock, Salinas, Calif.
Wilborn, Sam Werner, Austin, Texas.
Wingert, Willis A., Claremont, Calif.
Zenger, Doris Baker, East Hampton, N. Y.

ANNOUNCEMENTS

Forthcoming Examinations of American Board of Pediatrics, Inc.—The American Board of Pediatrics, Inc., will hold oral examinations on Oct. 9, 10 and 11, 1953, in Miami, Fla., and on Dec. 4, 5, and 6, 1953, in Indianapolis.

Symposium on Cardiovascular Physiology and Surgery.—Under the auspices of the Minnesota Heart Association, the University of Minnesota will present a Symposium on Cardiovascular Physiology and Surgery next Sept. 14 to 16 in the Museum of Natural History Auditorium on the university campus. A number of internationally known physiologists and vascular surgeons will participate. The symposium will be open, without tuition fee, to all physicians and to qualified investigators in the field of cardiac physiology. Housing accommodations will be available on the campus for out-of-town registrants who wish them. Further information may be obtained from the Director, Department of Continuation Medical Education, University of Minnesota Hospitals, Minneapolis 14.

Books

Angewandte Paediatrie: Ein Nachschlag—und Lesebuch für Studierende und Arzte. By Ernst Mayerhofer. Price, $20.40. Pp. 812, with 209 illustrations. Wilhelm Maudrich, Alserstr. 19, Wein VIII/65, 1952.

The author of this textbook has had unusual pediatric experience, having worked at first as an assistant in the University of Prague, then in Vienna, and finally, after the first world war, he became Professor of Pediatrics at the newly created Clinic in Zagreb, Yugoslavia.

This textbook is interesting and new in its approach. It is written not only for the student of medicine but particularly for the general practitioner in his role as a family physician. Although the author realizes that the modern trend in the practice of medicine is away from the family physician, still he is rather optimistic concerning a revival of this type of physician. The book is not greatly concerned with detailed descriptions of the symptoms of diseases, as a knowledge of these symptoms is, to a great extent, taken for granted. Mayerhofer rather wishes to guide the family physician in the evaluation, differential diagnosis, and, particularly, in the treatment of the disease as a whole. Nutritional problems as well as normal growth and development are considered in more detail. Of interest is the fact that Mayerhofer discusses the nutritional questions on the basis of the Pirquet system of nutrition. As a collaborator of Pirquet in the Hoover Relief Administration, he was able to accumulate a vast experience in this field. One hundred fifty-eight pages deal with the problem of nutrition.

The education and mental guidance of children, as well as the influences of the home and school, form the contents of the second chapter. Education and behavior difficulties, also the puberty period, are discussed from the family physician's viewpoint as an educator of children and as a school physician.

The third chapter contains a discussion of the importance of climate and clinical therapy. The author has made an intensive study in this direction. After a discussion of hereditary factors, the diseases of childhood are dealt with. The newborn period is a special favorite with the author, as Mayerhofer has been a leader in the study of allergy in the newborn period. The erythema toxicum neonatorum is an allergic phenomenon. In many instances breast-gland swelling and other clinical symptoms belong in this group of allergies.

It is unnecessary to point out that Mayerhofer discusses in a very interesting and original way all the other diseases of childhood, always keeping in mind the problems of the family physician. He deals with the question as to how the physician should act when treating a diseased child as well as how to combat the disease.

This reviewer enjoyed reading the book, and, since it is a textbook with a decidedly new approach, it would be well worth while if it would be translated into other languages. A translation into Spanish is contemplated.

Textbook of Refraction. By Edwin Tait, M.D. Price, $8. Pp. 418, with 93 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5, 1951.

Refraction is presented in this book in a rather different manner from that of most texts on this subject. As the author states, the book presupposes an existing knowledge of the anatomy of the eye and of the principles of optics, so that these subjects are not as fully developed as in previous standard texts. However, an unusually large amount of space is devoted to the physiology of the ocular muscles. The author particularly stresses the part of fusion and what he terms "vergence stimulus-response mechanism" in ocular muscle deviations. There is an extensive discussion of the role of accommodation in muscle imbalance, including the diagnosis and treatment of the various types. He particularly condemns the use of base-out prisms as advocated by some in the treatment of esotropia in children.

Less than one-third of the book is devoted to refraction itself, but there is a good presentation of various techniques used in both objective and subjective methods. Many helpful pictures of instruments and charts are included to illustrate the various means presented. The Tait method

of dynamic skiametry with the instrument developed by the author is particularly stressed, though it is not widely used. A suggested system of refraction is included, giving in outline form techniques of testing with an interpretation of the findings.

The author emphasizes that the refractionist is dealing with a "dynamic organism, the living body," and that lens corrections are never exact but must be determined by a careful correlation of various methods of refraction combined with a determination of the state of the neuromuscular mechanism.

Fathers Are Parents Too. O. Spurgeon English, M.D., and Constance J. Foster. Price, $3.75. Pp. 304. G. P. Putnam's Sons, 210 Madison Ave., New York 16, 1951.

The authors of "Fathers Are Parents Too" are very well qualified to write the book. Dr. O. Spurgeon English is a professor of psychiatry at Temple University in Philadelphia. Probably its readability (and minimum of profuse verbiage) is due to his collaboration with Mrs. Constance J. Foster, an excellent free-lance authoress, used to writing for lay publications.

Like the womb-to-tomb indoctrination policy of some foreign governments, this volume indoctrinates the father while the infant is still a "gleam in the father's eye."

The authors cover the child's infancy, childhood, adolescence, and dating and mating periods, and advise the father how to conduct himself from the time he first learns of his wife's pregnancy through the grandfather experience.

The premise of the book is that fathers should be educated to modern psychological orientations toward their families and must take an active part in rearing their children in order to fulfill their obligation to family life. They contrast the successful father with the despot and the type of man who feels he has done his share if he supplies the financial needs adequately.

Each age group and problem discussed is covered very fully with good examples of how to put the principles to work. The security of the child is the main concern of the authors. As an example, the security of the mother in knowing that her husband is welcoming the birth of the child is given a whole chapter. The experienced father is given just as much consideration as the man who is preparing for his first offspring.

Although the whole book is excellent, the best of it comes last in a chapter entitled "It's Never Too Late." So many parents have had the experience of reading books or attending lectures and finishing with the frustrated wish to start all over again. This chapter does away with the "I'm hopeless and have done everything wrong" feeling very successfully. It not only preaches the doctrine of improving a bad situation, it gives very concrete advice on tackling a wide variety of problems.

Unless one has a deep-seated and dogmatic objection to the psychoanalytical viewpoint, this is an excellent book to own and recommend to parents and those planning to be parents.

CORRECTION

In the November, 1952, issue, page 675, in the review of the book titled "Child Rorschach Responses: Developmental Trends from Two to Ten Years," by Ames, Learned, Metraux, and Walker, the Gesell Institute of New Haven, which is a private organization, is incorrectly referred to as the Gesell Institute of Child Development at Yale University. Dr. Gesell is no longer connected with Yale University in an active capacity, and the Clinic of Child Development, of which he was director, ended its function in 1948, with his retirement.

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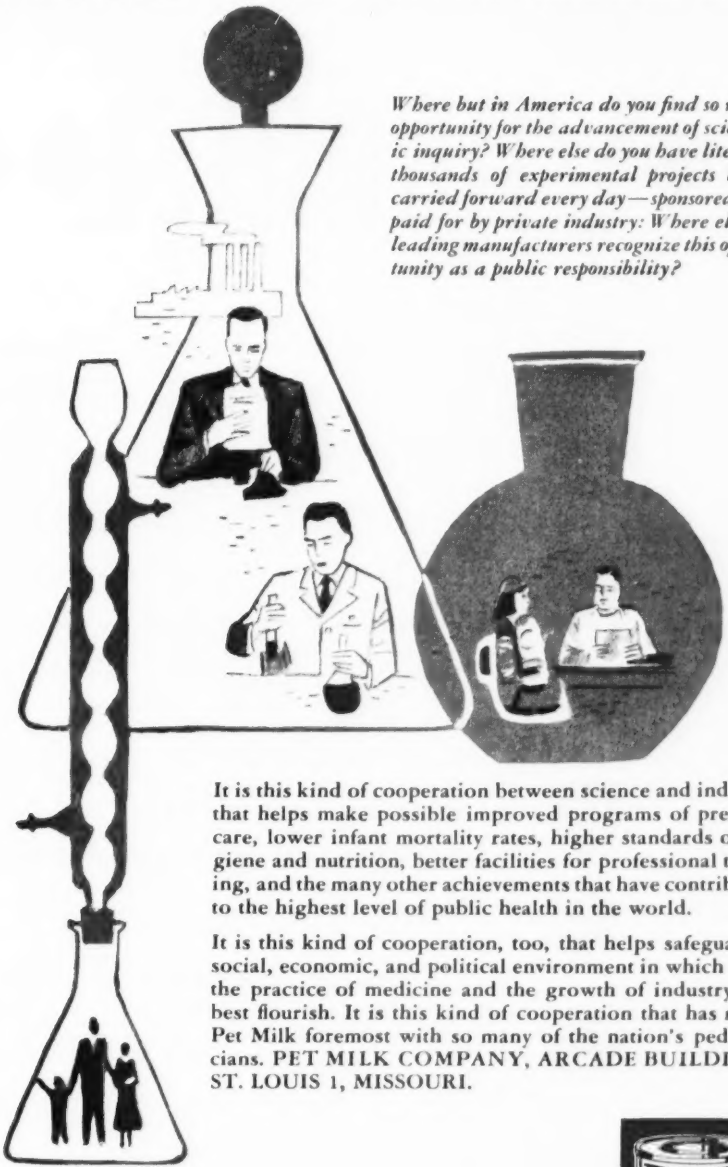

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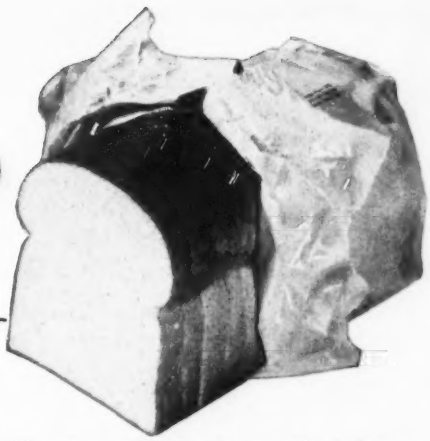

Some twelve years ago the baking industry began large-scale, nationwide commercial production of enriched breads. Today such breads represent about three-fourths or more of all the marketed white bread in the United States,[1] and rank high among the foods which contribute essential nutrients—in important amounts—at low cost—to the nutrition of the American people.[2]

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*Daily dietary allowances recommended by National Research Council for a sedentary man (154 lb.).

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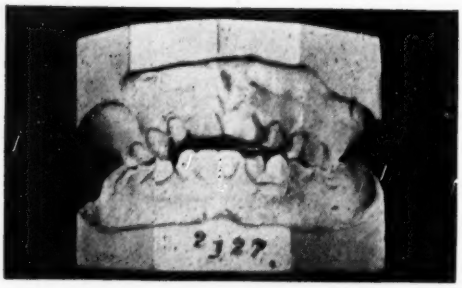
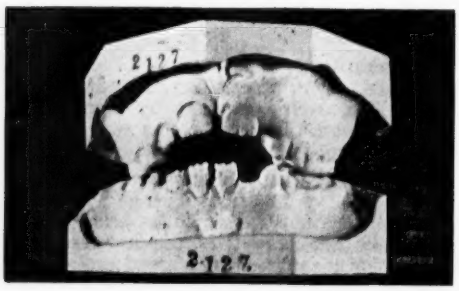
1. Geddes, W.F.: Cereal Chemists Guard Nutrition, Agricultural and Food Chemistry *1*:38 (Apr.) 1953.
2. Sherman, H.C.: Chemistry of Food and Nutrition, ed. 8, New York, The Macmillan Company, 1952, pp. 597-600; 646.
3. Flour and Bread Enrichment, 1949-50: Prepared by The Committee on Cereals, Food and Nutrition Board, National Research Council, 1950.
4. Sherman, H.C.: The Nutritional Improvement of Life, New York, Columbia University Press, 1950, pp. 86-87.
5. Bakery Products; Definitions and Standards of Identity: Federal Register *17*:4453 (May 15) 1952.
6. Data furnished by the Laboratories of The American Institute of Baking, Chicago, Illinois.
7. Watt, B.K., and Merrill, A.L.: Composition of Foods—Raw, Processed, Prepared; United States Department of Agriculture Agriculture Handbook No. 8, 1950.



Four year old girl whose habit of putting fingers in mouth caused separation.



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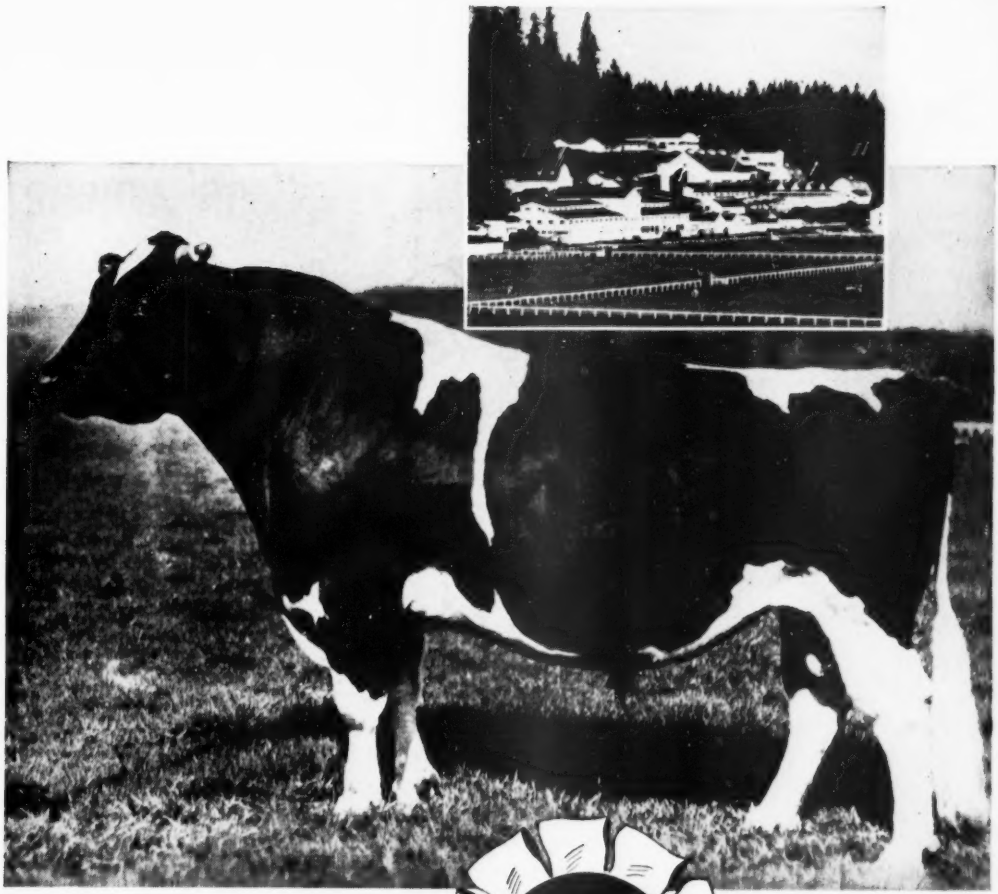

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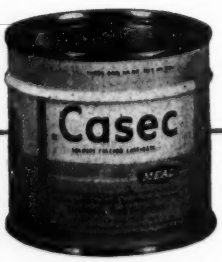

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Measuring the dose is uncomplicated . . . Because it is a clear solution, accurate measurement of Globin Insulin depends only upon understanding the markings on the syringe. The solution is ready to use at any moment; its homogeneity does not depend upon the patient's skill or judgment.

Sleep is not likely to be disturbed . . . When a single daily dose of Globin Insulin is given first thing in the morning its maximum action occurs in the afternoon and evening when it is most needed; any tendency to hypoglycemia at this time is readily recognized and offset. The action wanes during the night, therefore nocturnal hypoglycemic reactions are unlikely to occur.

Globin Insulin 'B.W.&Co.'®

40 and 80 units per cc. vials of 10 cc.

Burroughs Wellcome & Co. (U.S.A.) Inc.

Tuckahoe 7, N. Y.

Dispersible

DRISDOL®

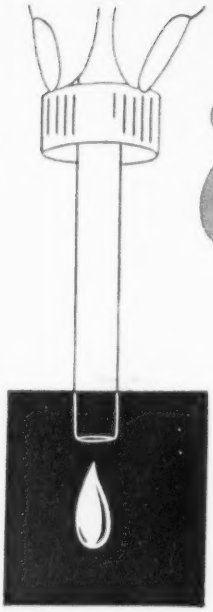
WITH

VITAMIN A

COMPLETELY

Milk

Diffusible



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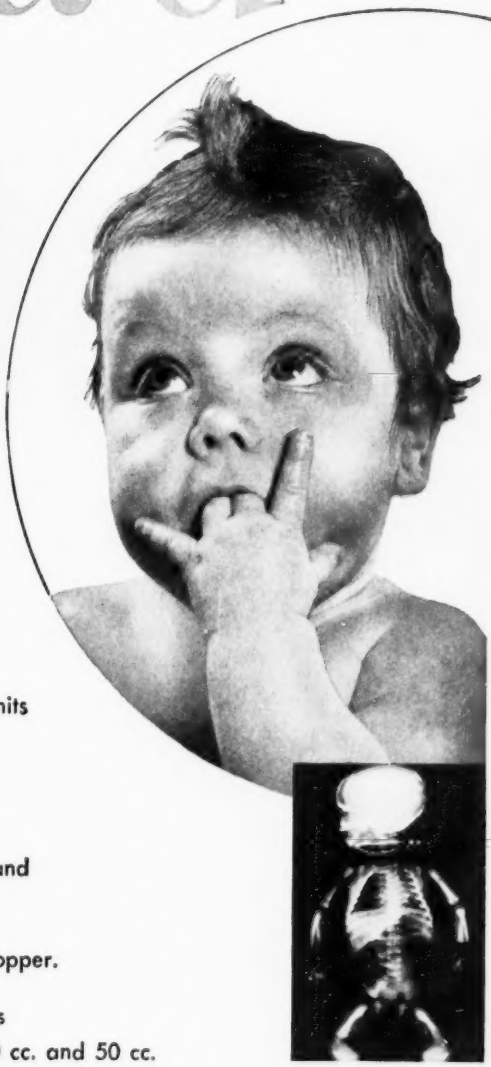

Drisdol with Vitamin A administered in milk becomes an integral part of the child's diet. It diffuses completely in milk, orange juice and other liquids without an oily film, does not separate, float or tend to adhere to nursing bottle or nipple. May also be given on the tongue or in solid foods.

Drisdol with Vitamin A contains per gram 50,000 units of vitamin A and 10,000 units of crystalline vitamin D_2 (calciferol). Each drop delivers 1250 vitamin A units and 250 vitamin D units.

Dosage for infants, 2 drops; for older children and adults, from 4 to 6 drops daily in milk.

Supplied in bottles of 10 cc. and 50 cc. with dropper.

Also Drisdol in Propylene Glycol (10,000 units of vitamin D_2 per gram) in bottles of 5 cc., 10 cc. and 50 cc.

To help build a sound structure and promote growth

Drisdol, trademark reg. U. S. & Canada, brand of crystalline vitamin D_2 (calciferol)

Winthrop-Stearns INC.

NEW YORK, N. Y. WINDSOR, ONT.